The University of Melbourne

School of Botany

G27 Botany New Building, 3rd March 2009

Rudi Lemberg Lecture 2009

Genes in organelles

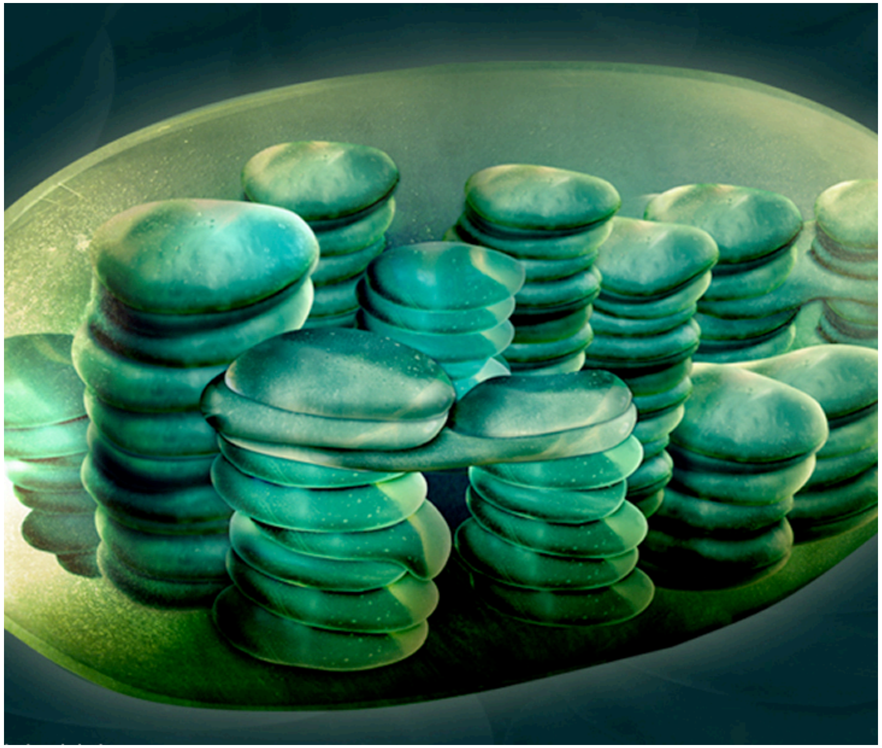
Mitochondria, ageing, and sex – energy versus fidelity

John F. Allen

School of Biological and Chemical Sciences, Queen Mary, University of London

www.jfallen.org

Queen Mary
University of London



Rudi Lemberg Lecture
Prof John Allen

Prof JF Allen
John Allen is Professor of Biochemistry at Queen Mary, University of London. John's principle interest is photosynthesis, the process by which plants and algae convert light, water and carbon dioxide into sugars and oxygen. He has revolutionized our understanding of how photosynthesis evolved and contributed fascinating new hypotheses about the origin of the two-part photosynthesis in bacteria. John has also developed new hypotheses about the endosymbiotic origin of photosynthesis in plants and algae, which also predict why humans age.

Title: Genes in organelles. Mitochondria, ageing, and sex - energy versus fidelity

When: 3 March 2009 - 5PM

Where: G27 Botany New Building

Time: 5pm-6pm

Other: Refreshments will be served after the lecture.

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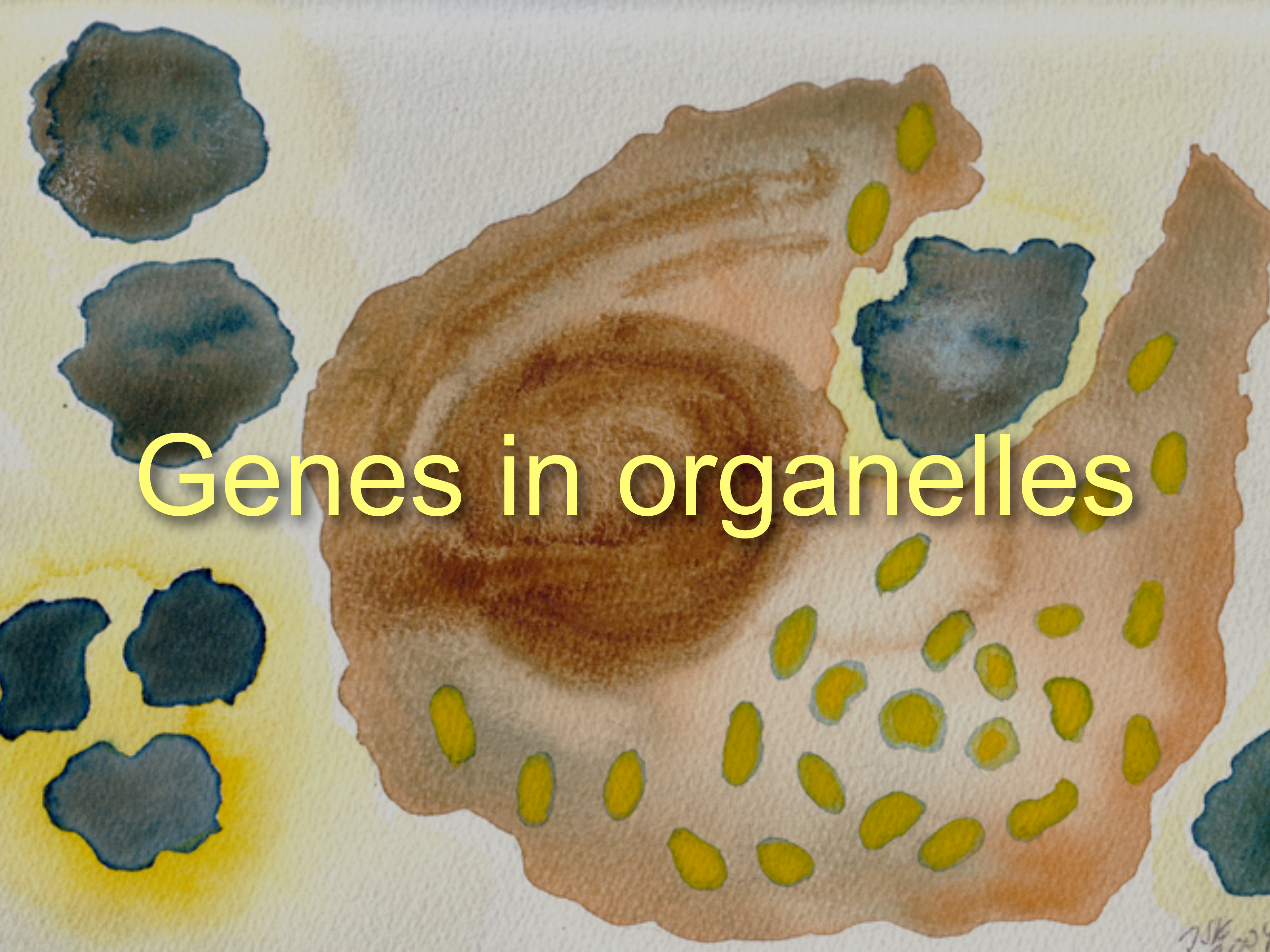
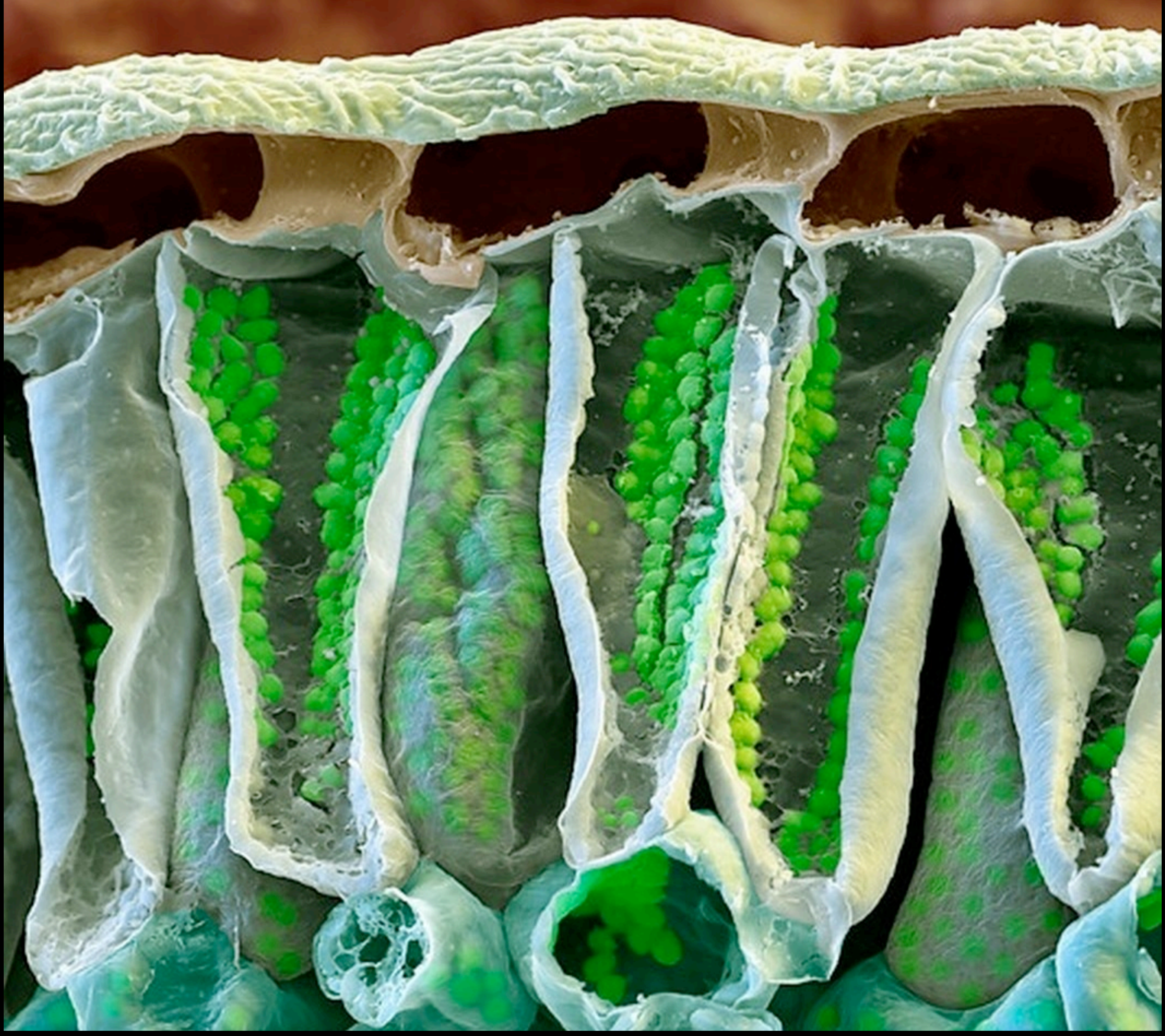
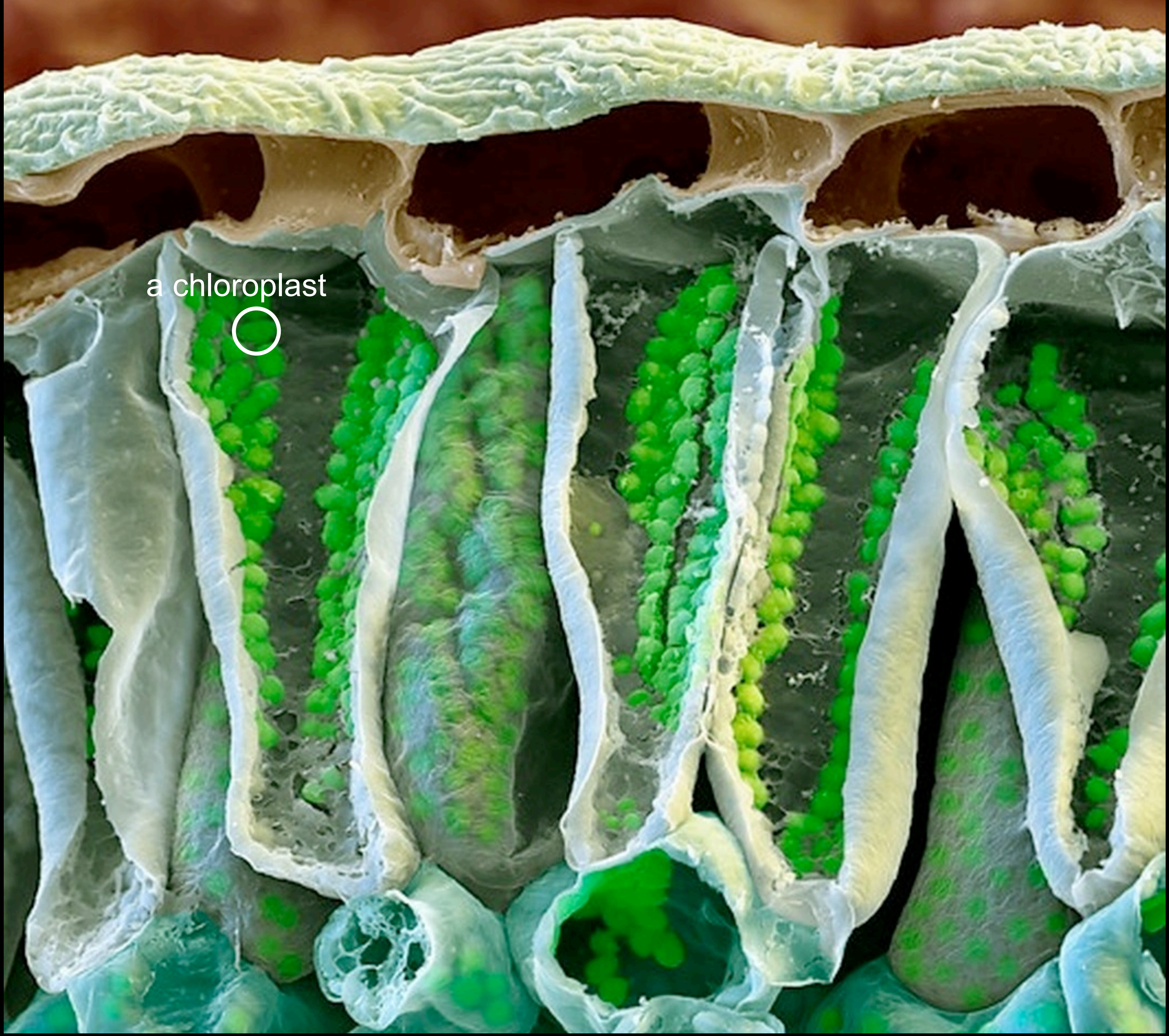
Max Rudolph Lemberg

1896-1975

Genes in organelles

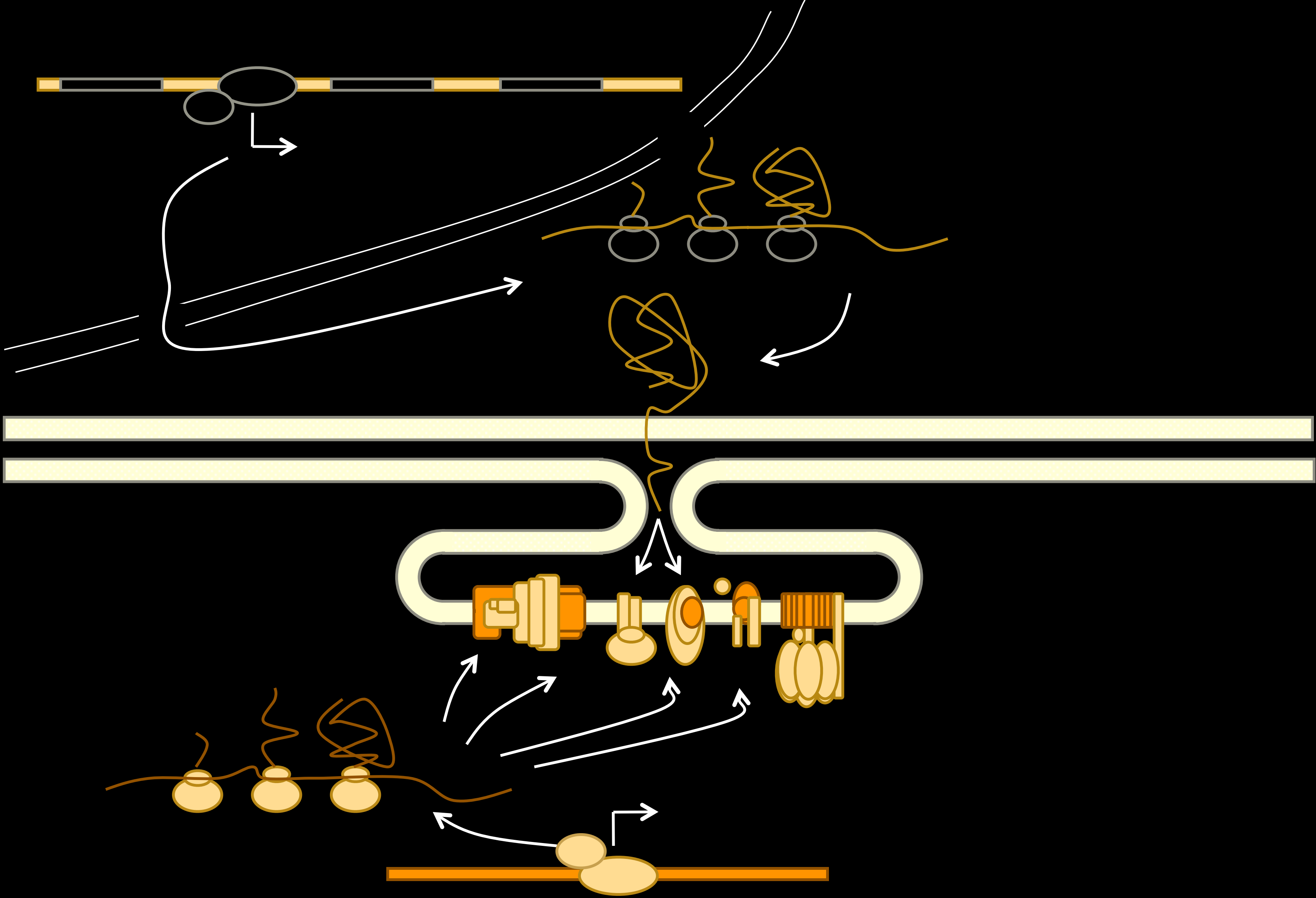


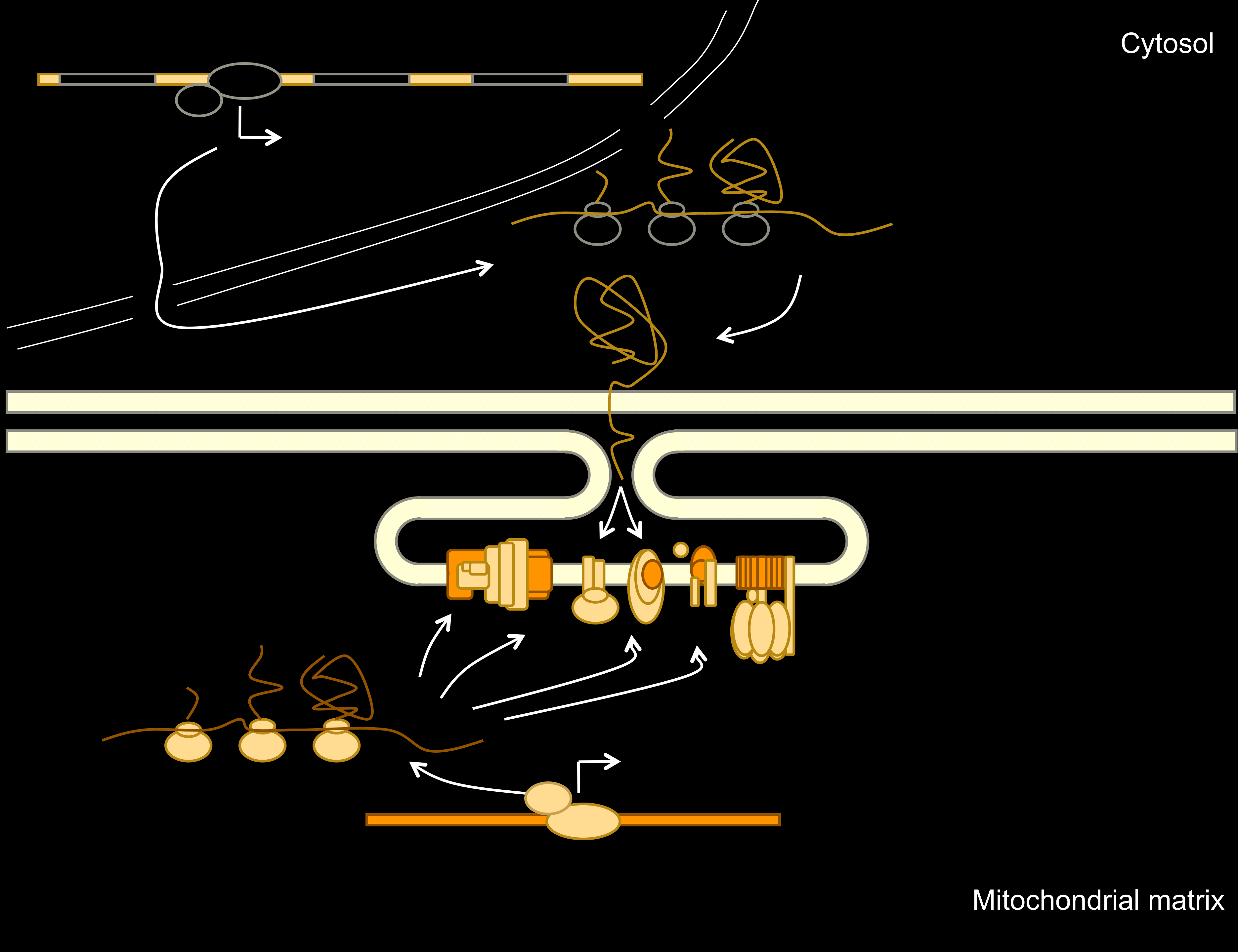

‘Christmas-Rose’ leaf SEM cross-section; Science Photo Library (SPL)

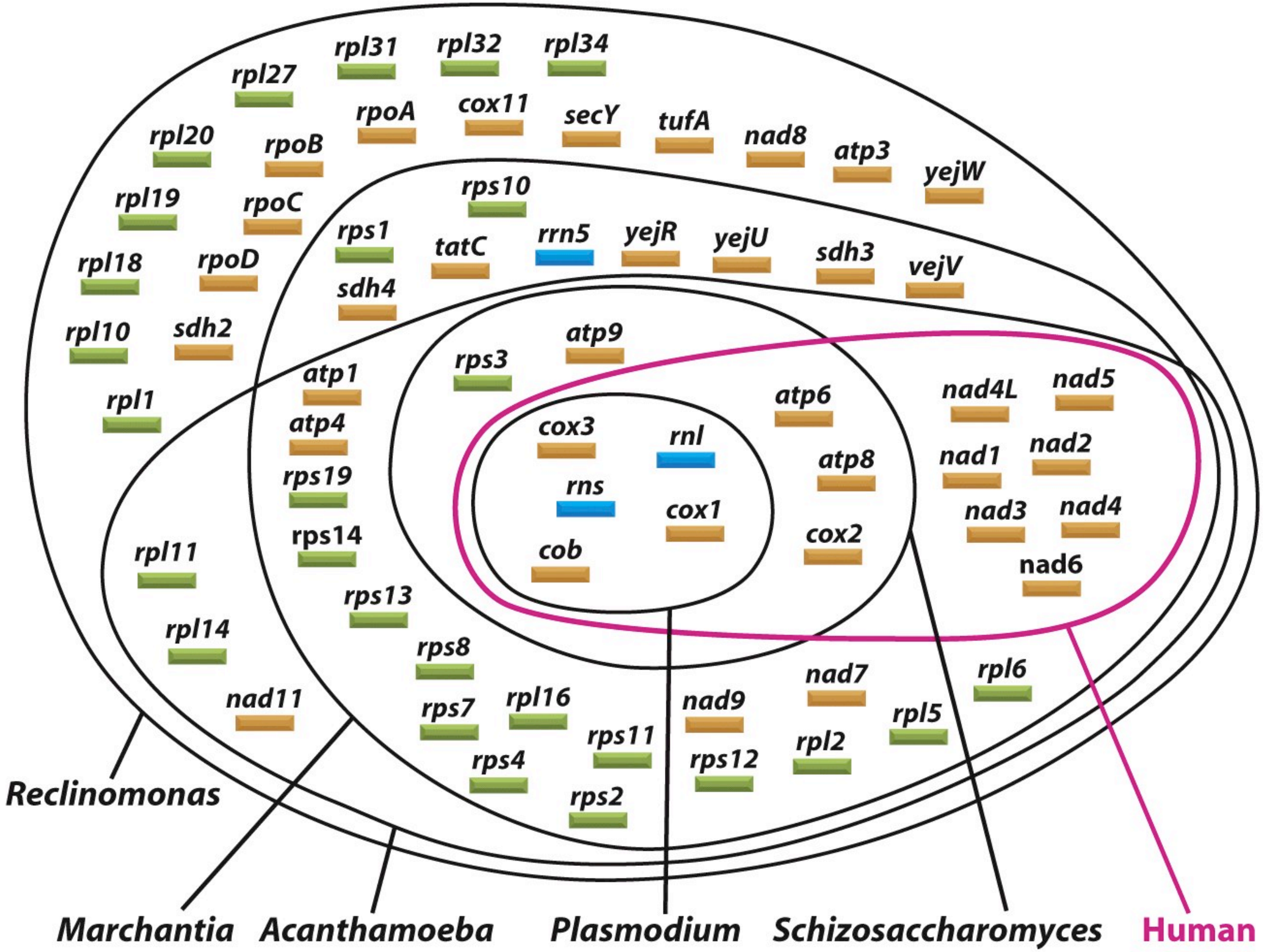


‘Christmas-Rose’ leaf SEM cross-section; Science Photo Library (SPL)

A mitochondrion—one of many tiny power-houses within cells that control our lives in surprising ways

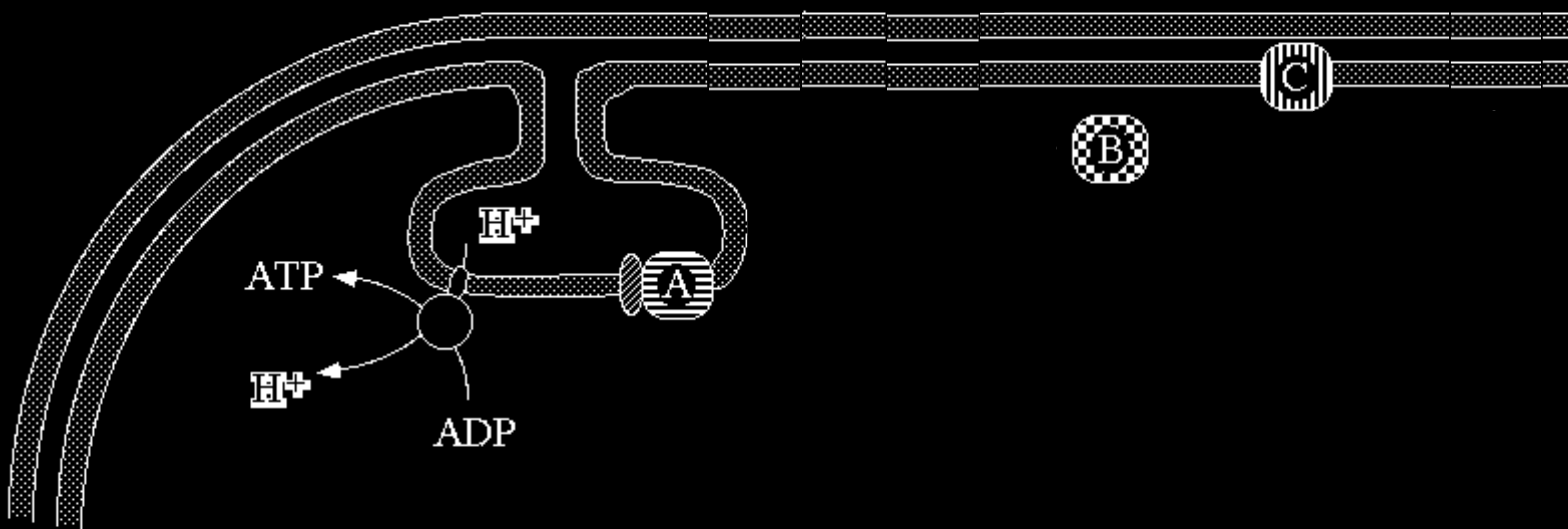



Cytosol
Mitochondrial matrix

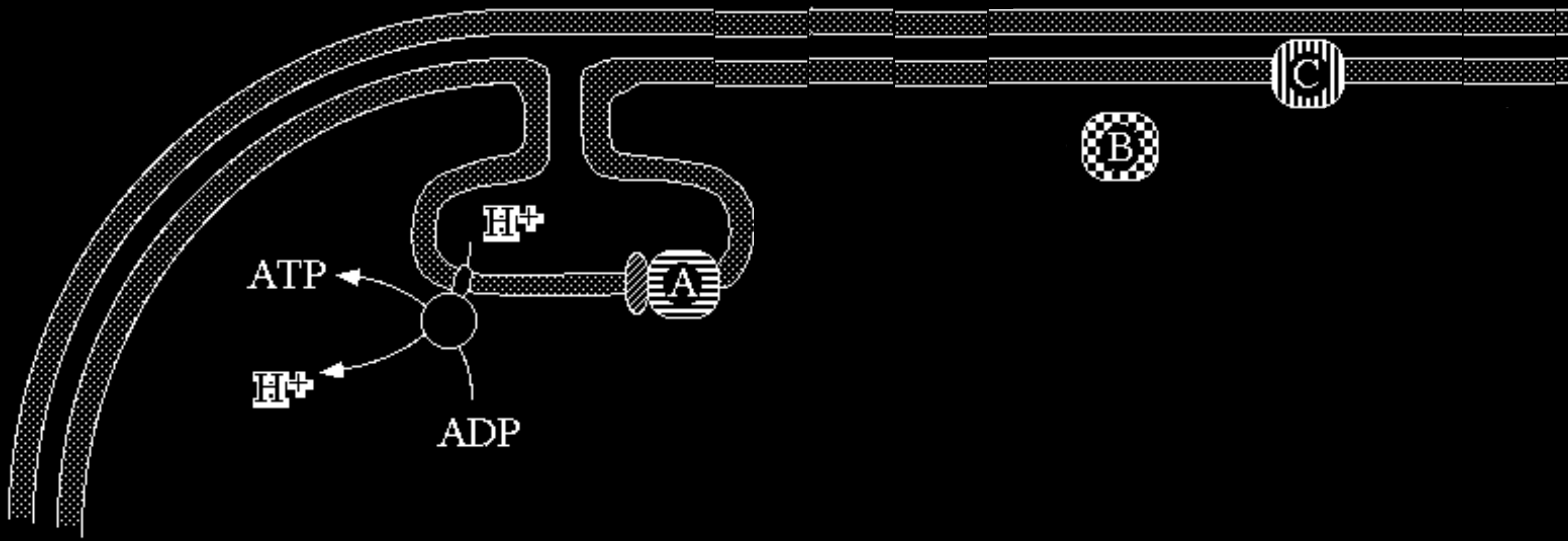


Comparison of mitochondrial genomes

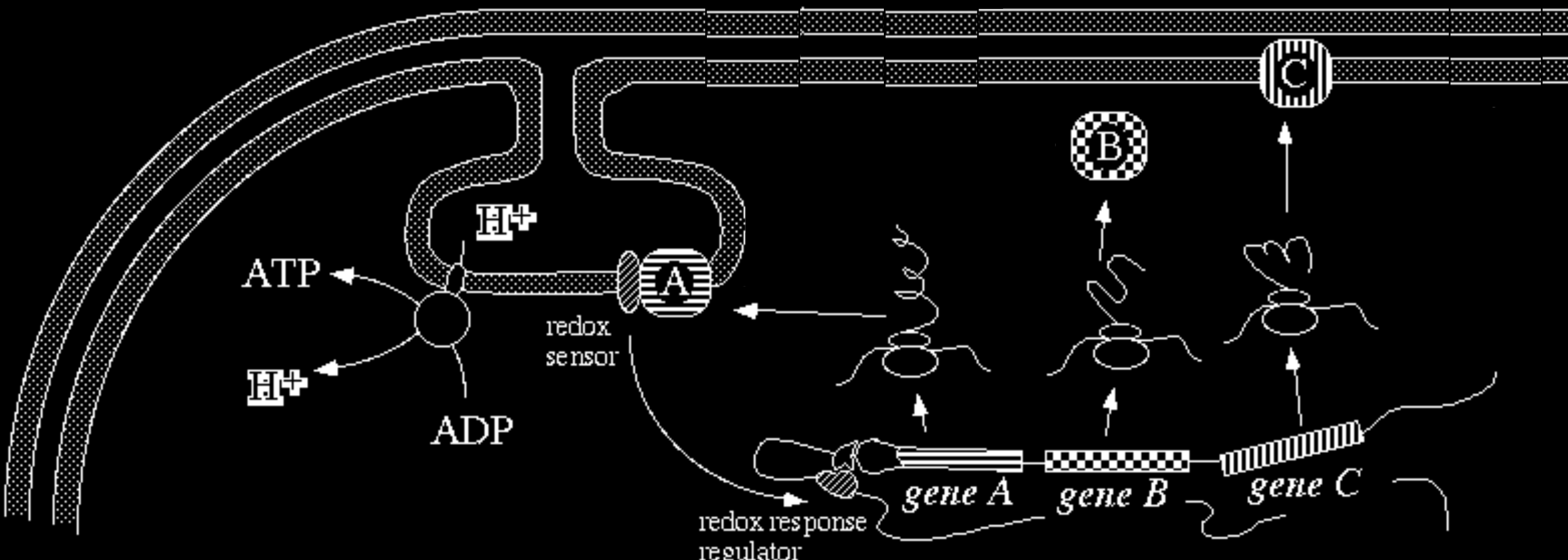
Less complex mitochondrial genomes encode subsets of the proteins and ribosomal RNAs that are encoded by larger mitochondrial genomes. There are only four genes present in all known mitochondrial genomes; these encode ribosomal RNAs *(rns* and *rnl),* cytochrome *b (cob),* and a cytochrome oxidase subunit *(cox1).* Adapted from M.W. Gray et al., *Science* 283:1476-1481, 1999. With permission from AAAS.



H+
ATP
H+
ADP
A
B
C

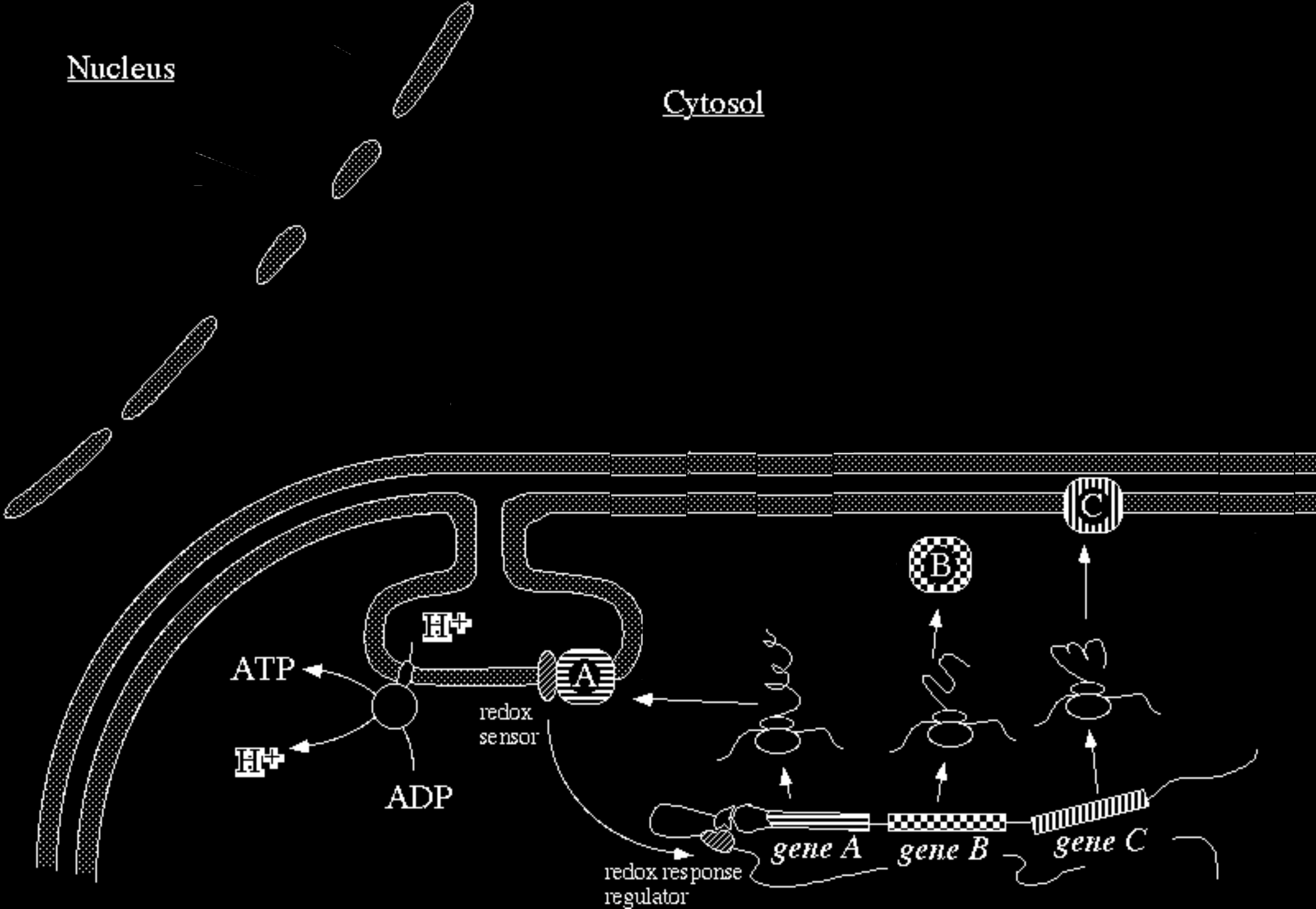


Bacterium

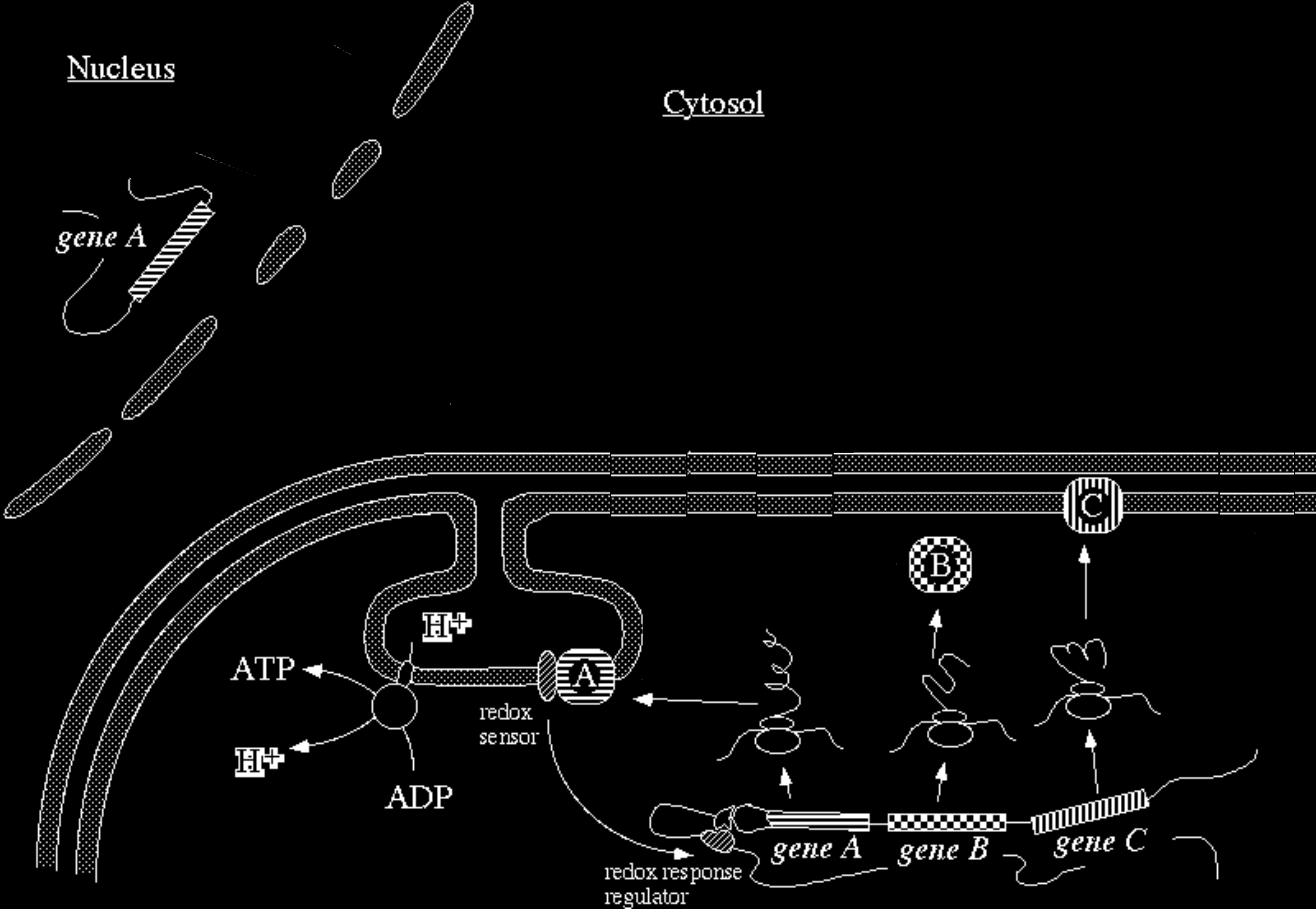


C
B
H+
ATP
A
redox
sensor
H+
ADP
gene A
gene B
gene C
redox response
regulator

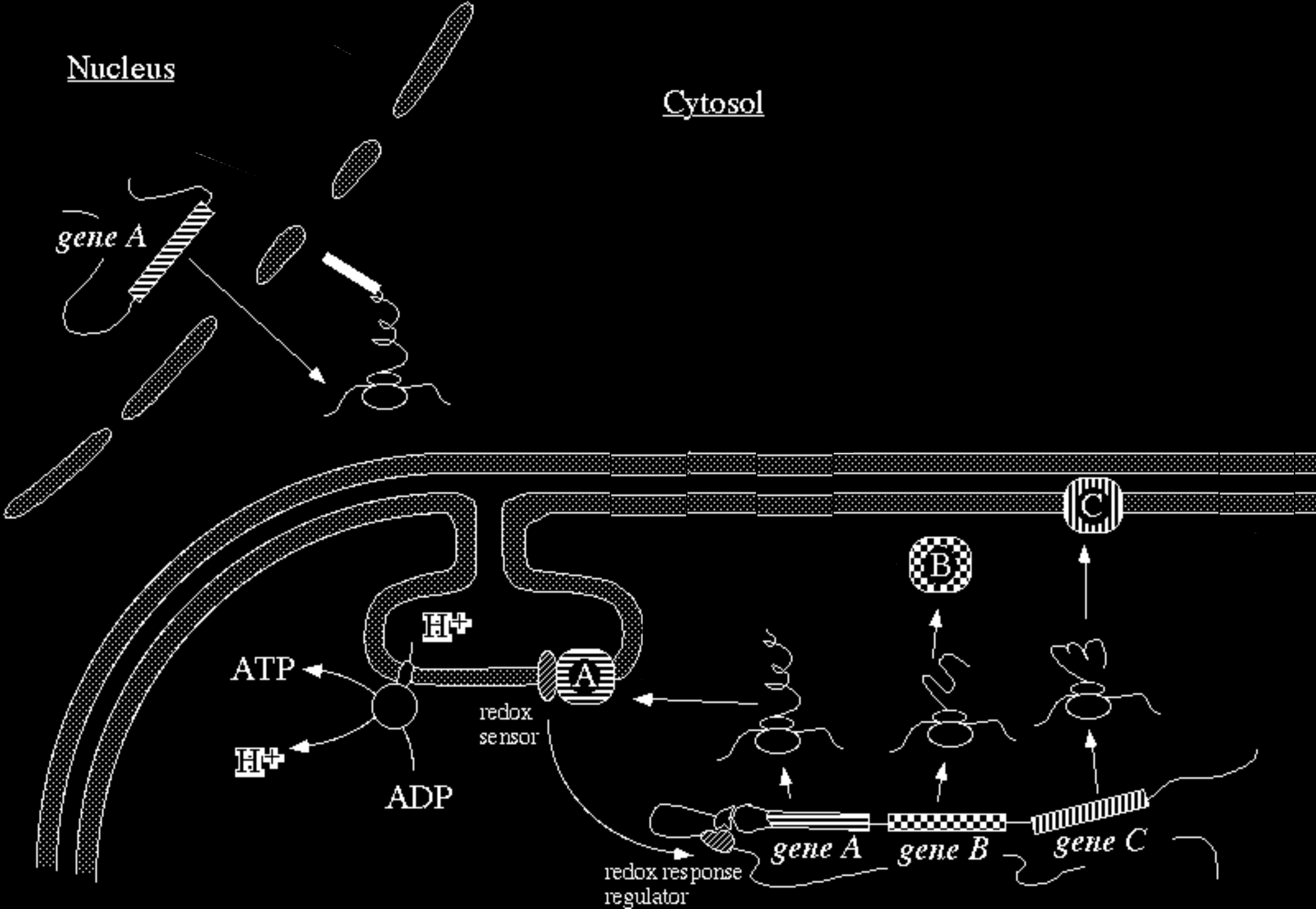
Bacterium



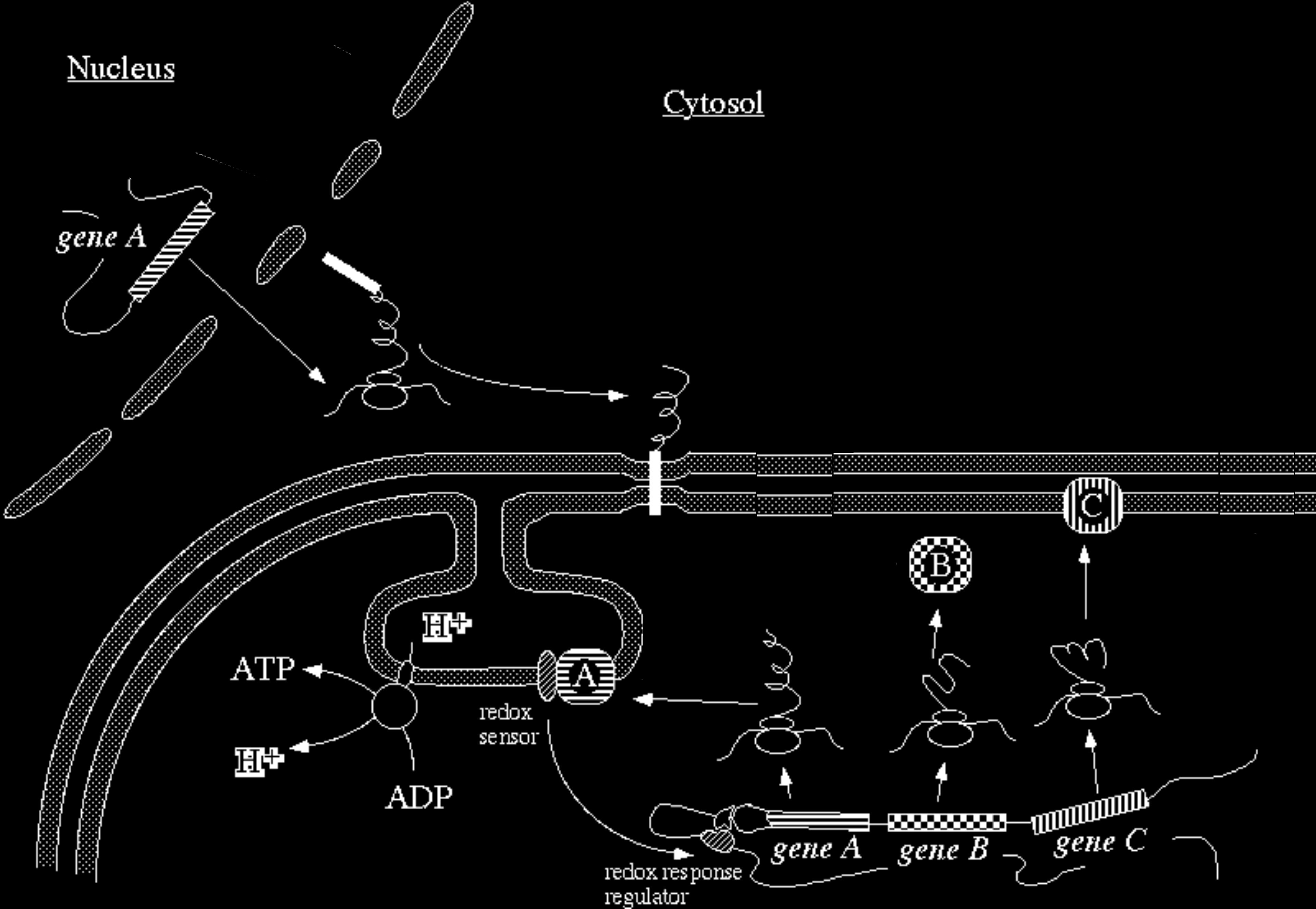
Endosymbiont



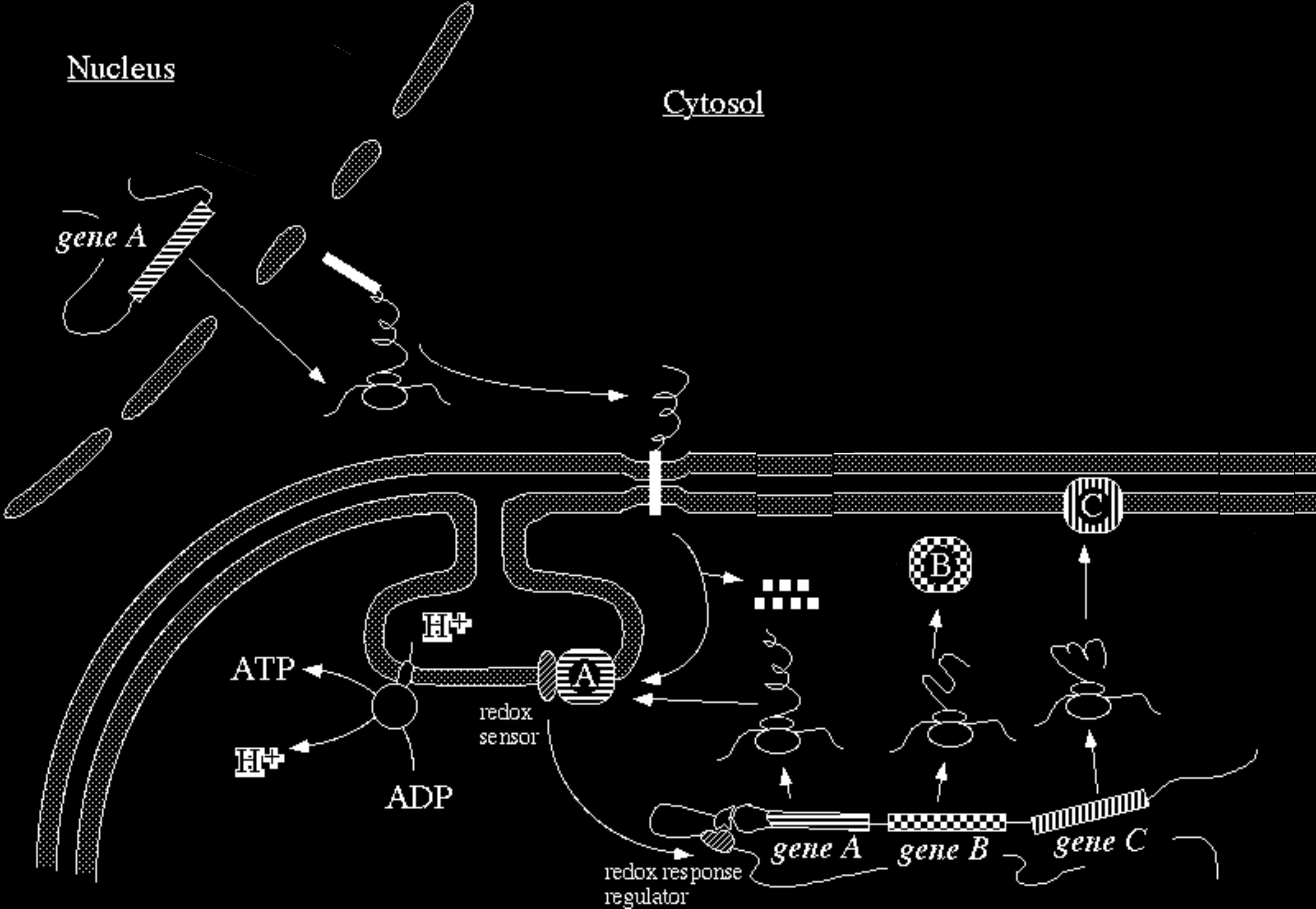
Endosymbiont



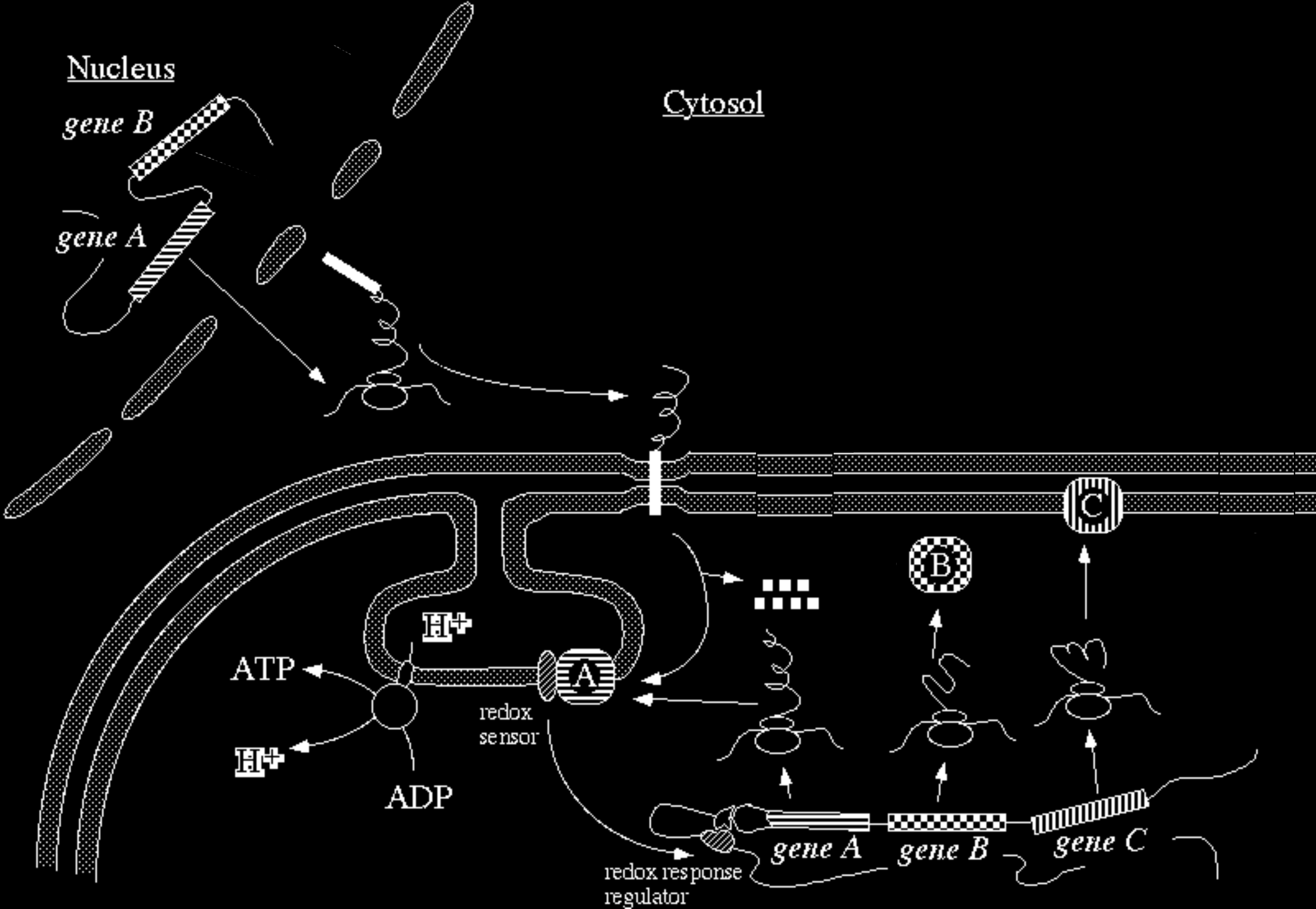
Endosymbiont



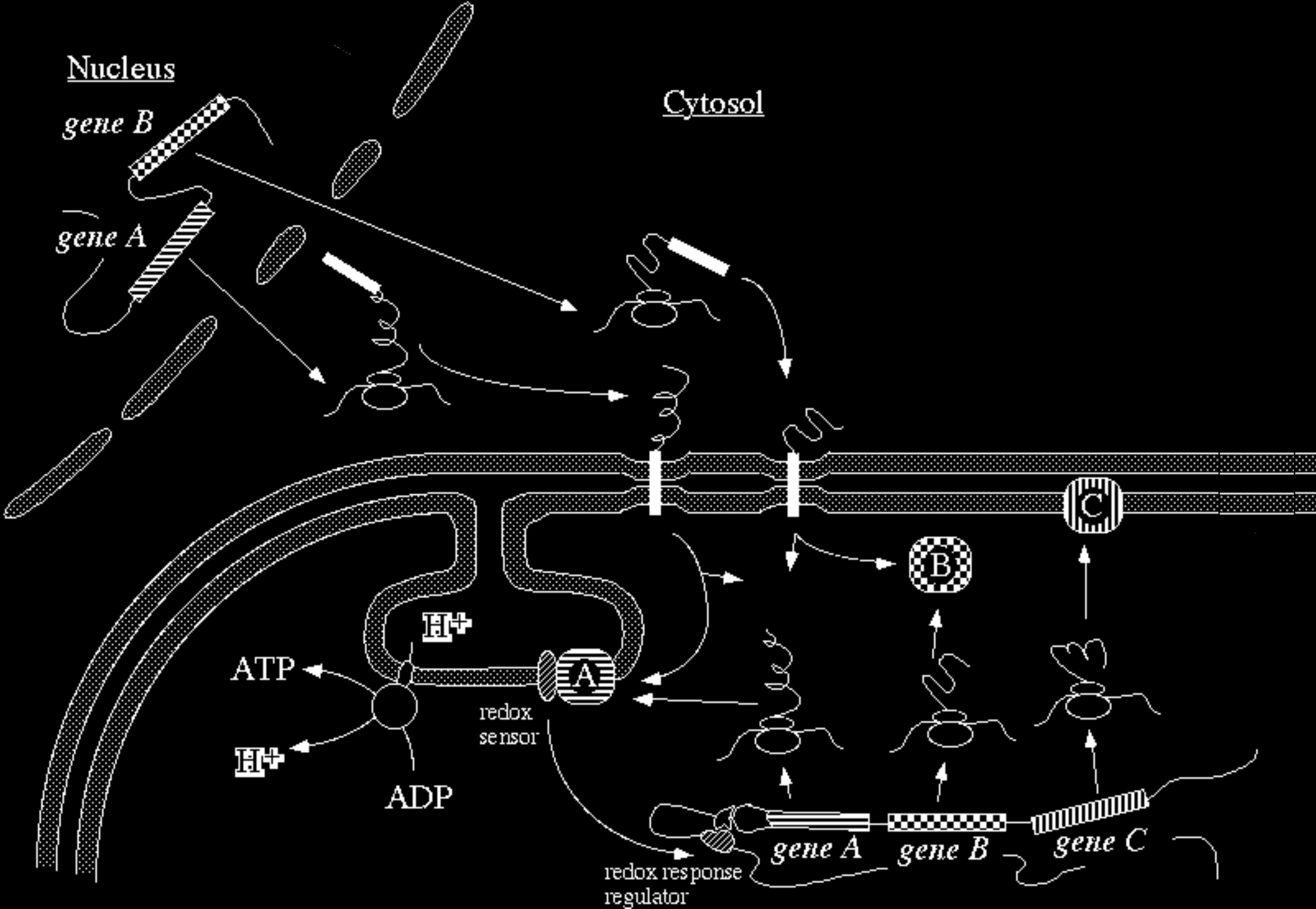
Endosymbiont



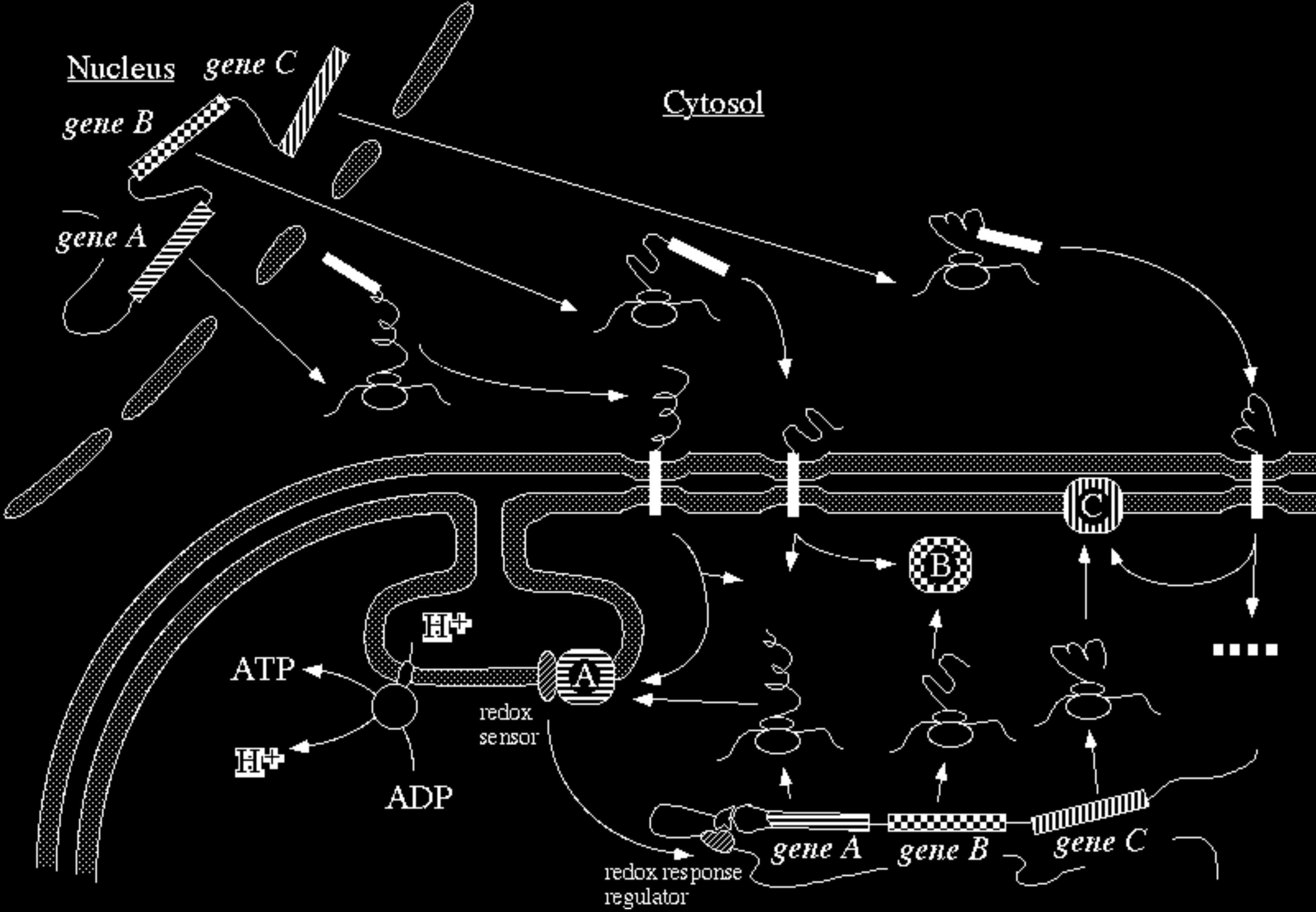
Endosymbiont



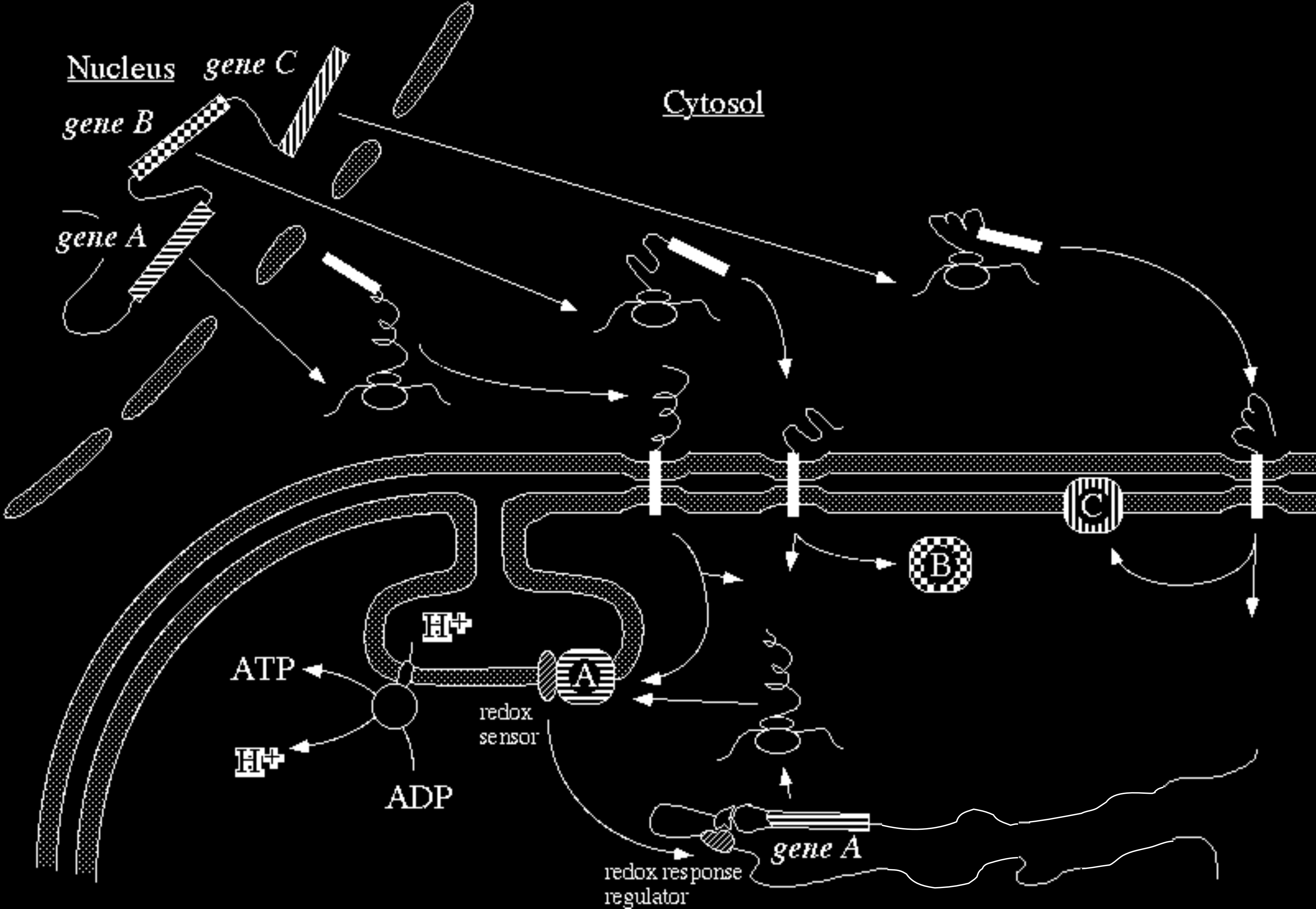
Endosymbiont



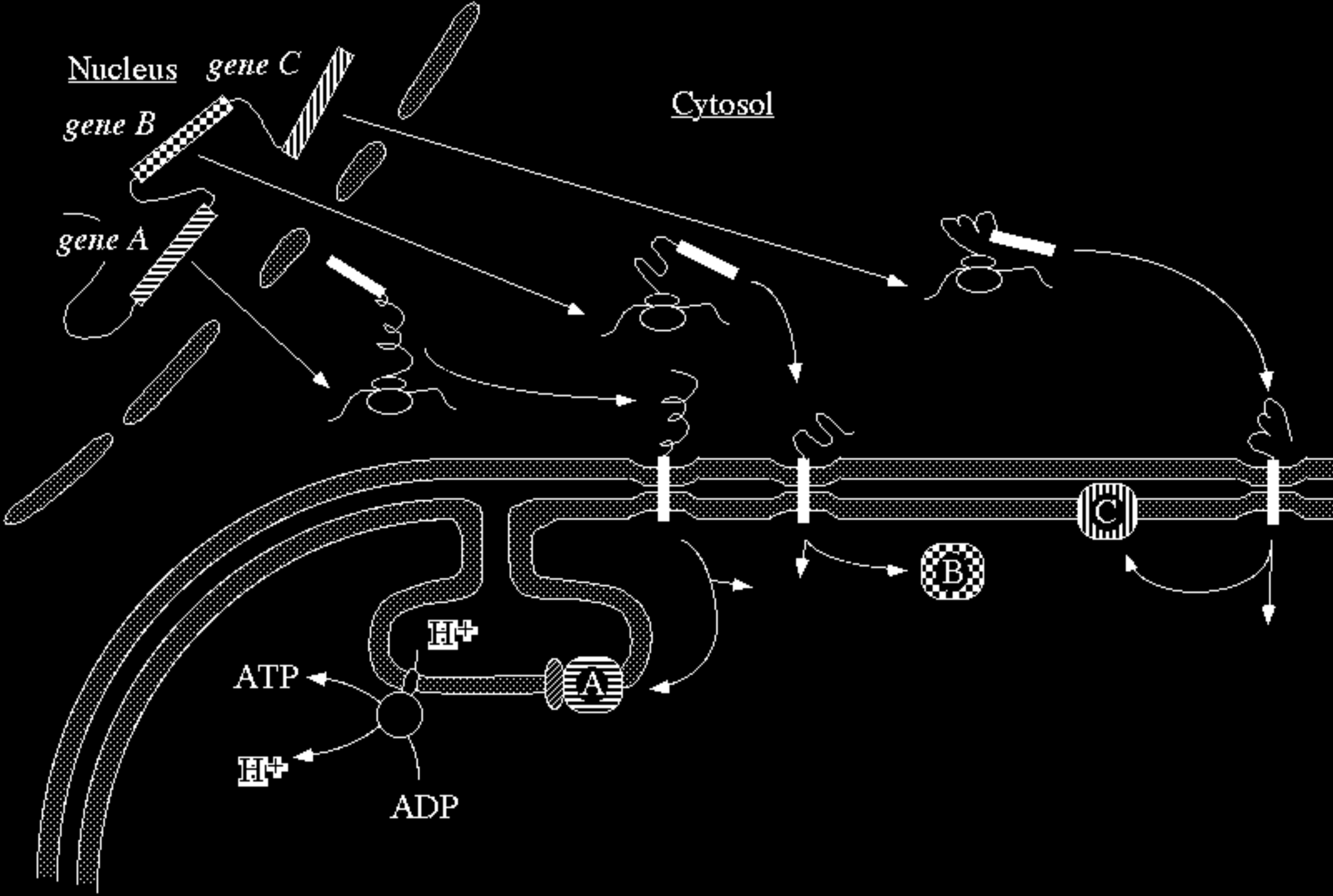
Endosymbiont



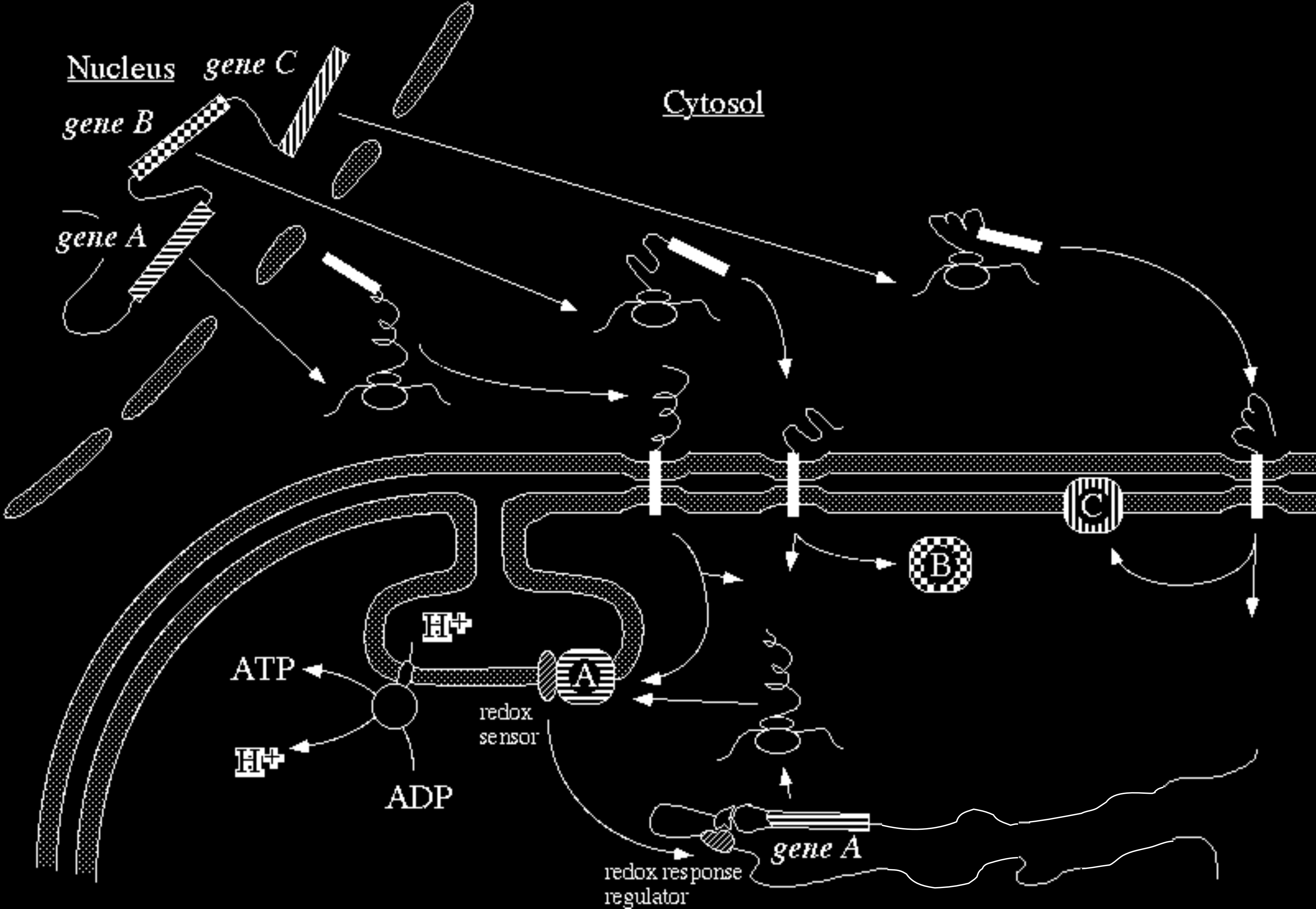
Endosymbiont



Endosymbiont



Endosymbiont



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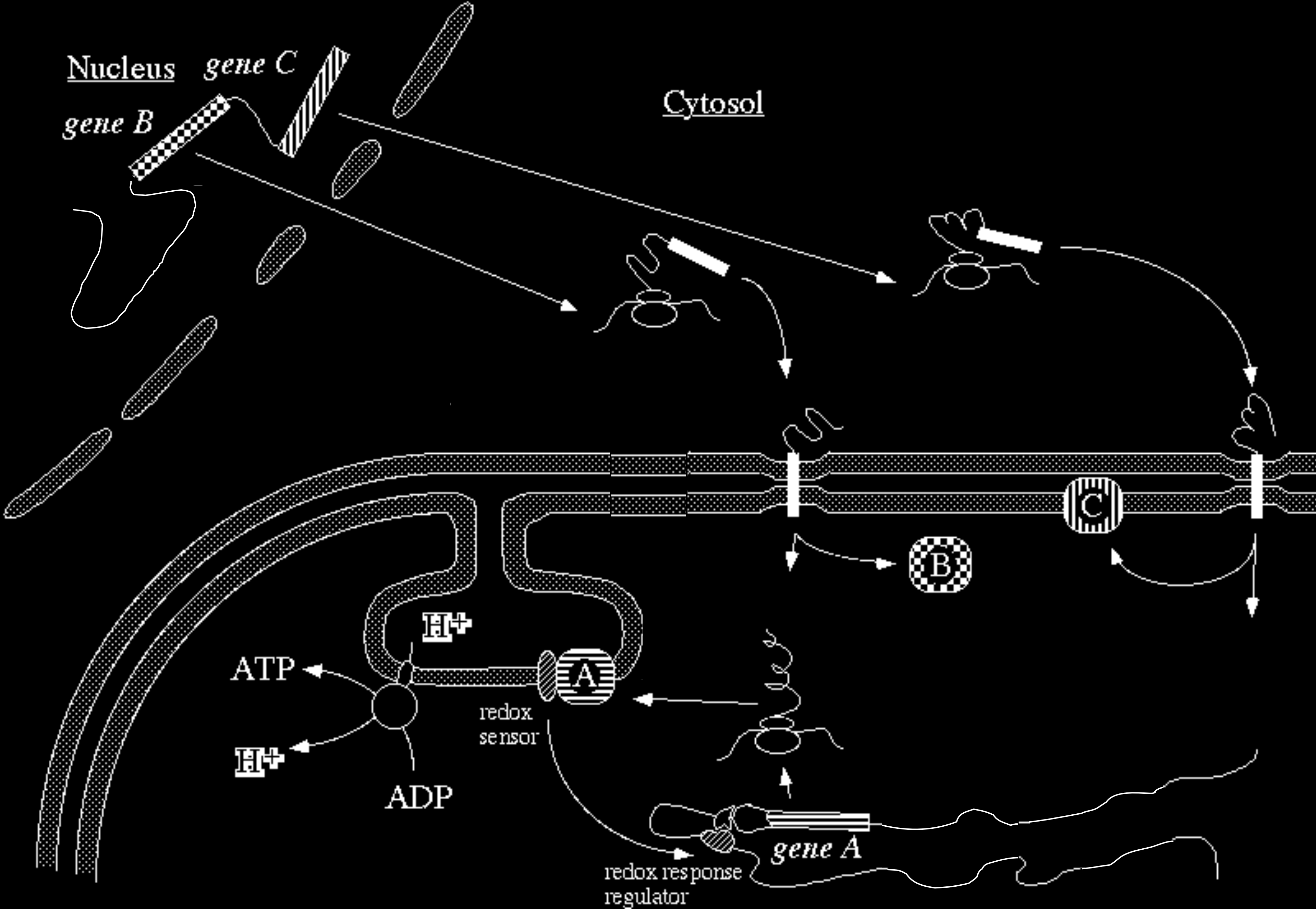
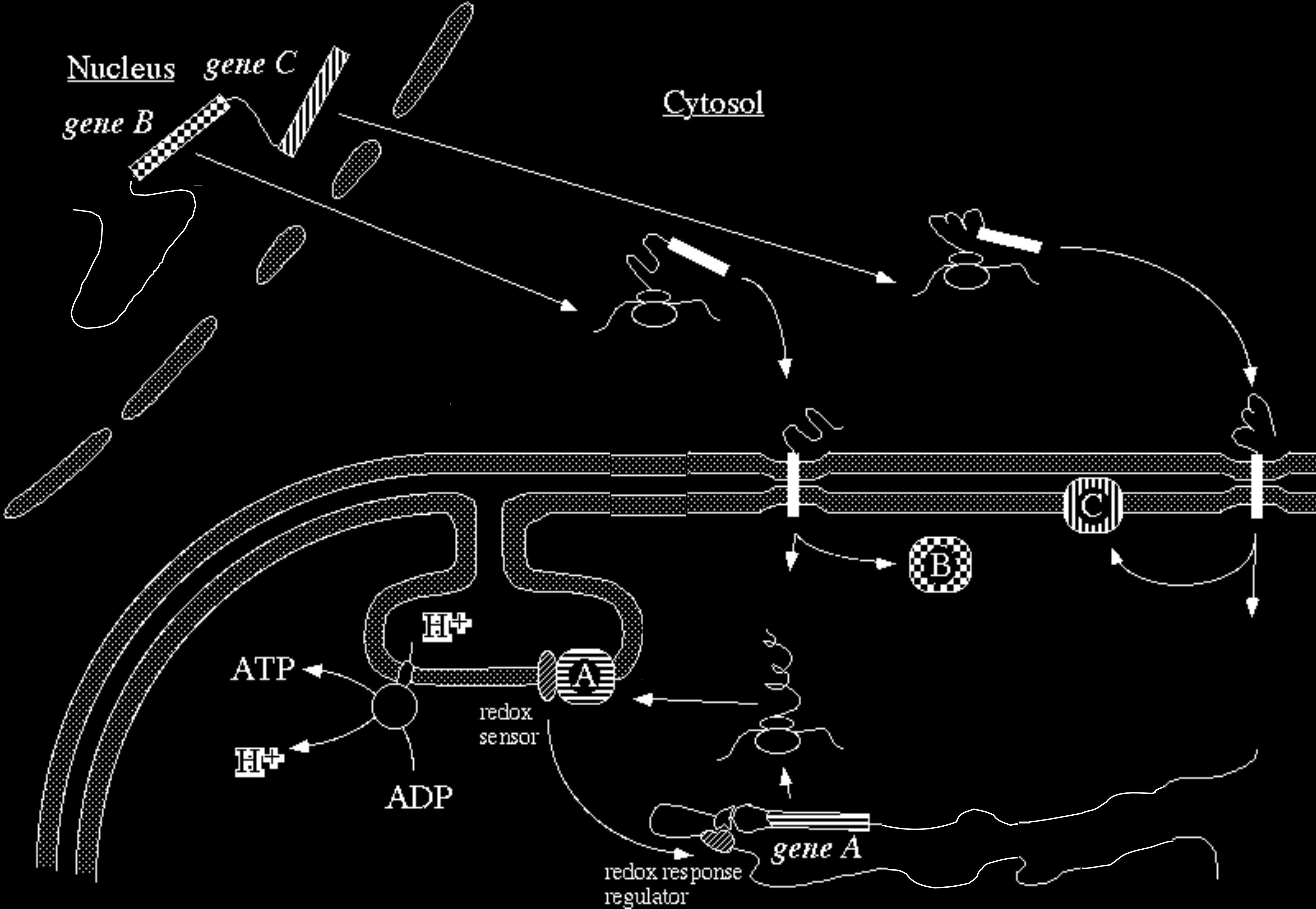
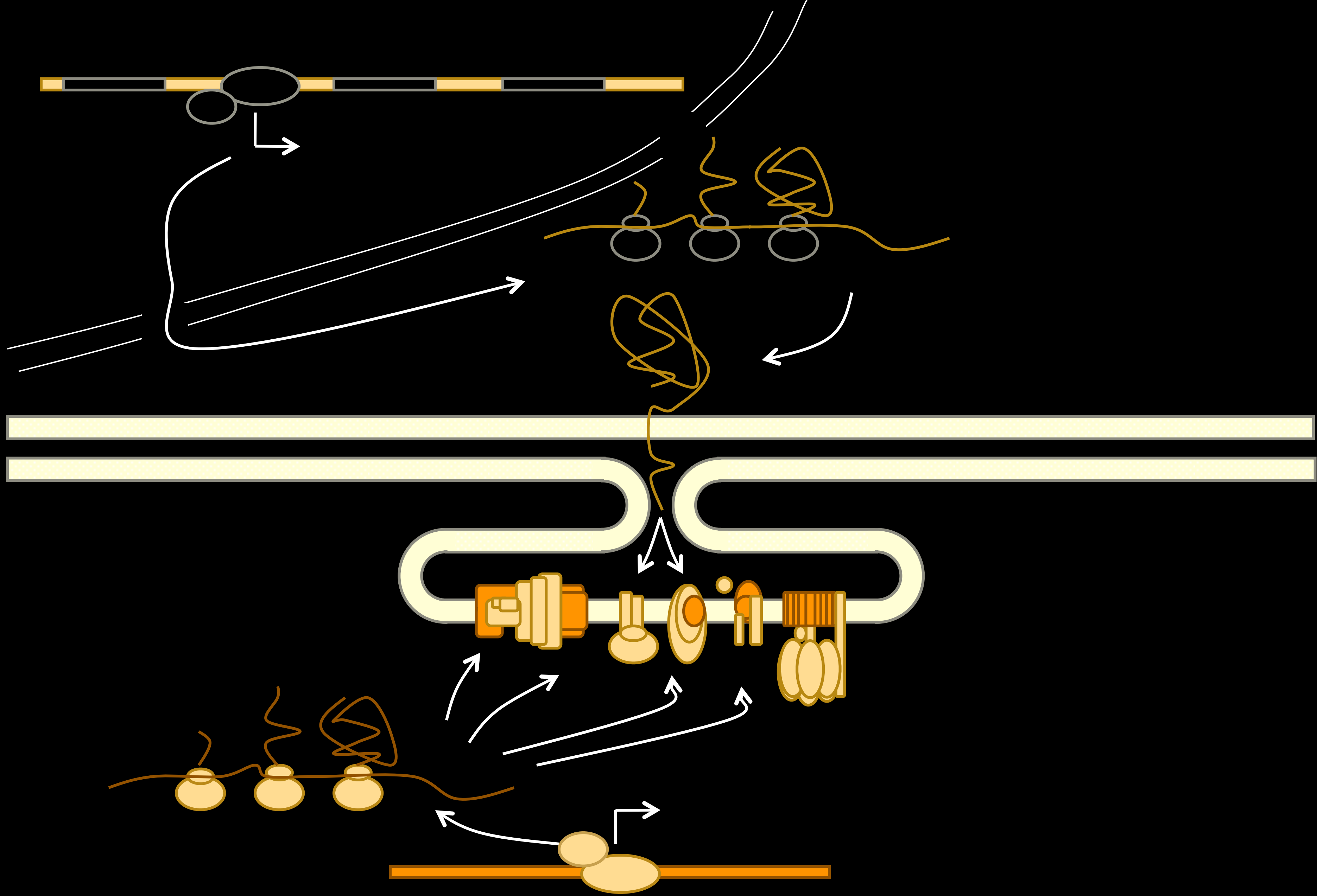


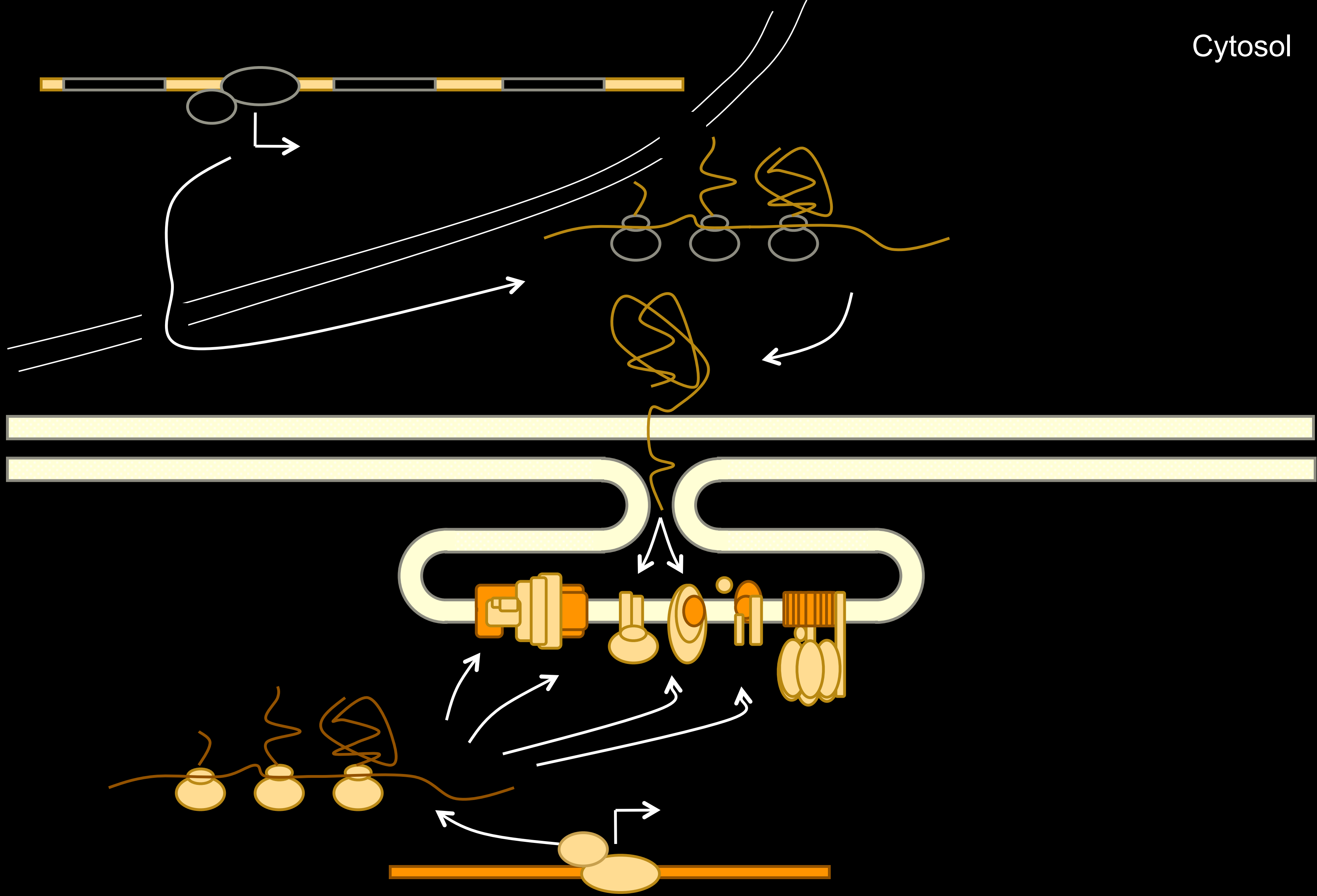
Bioenergetic organelle

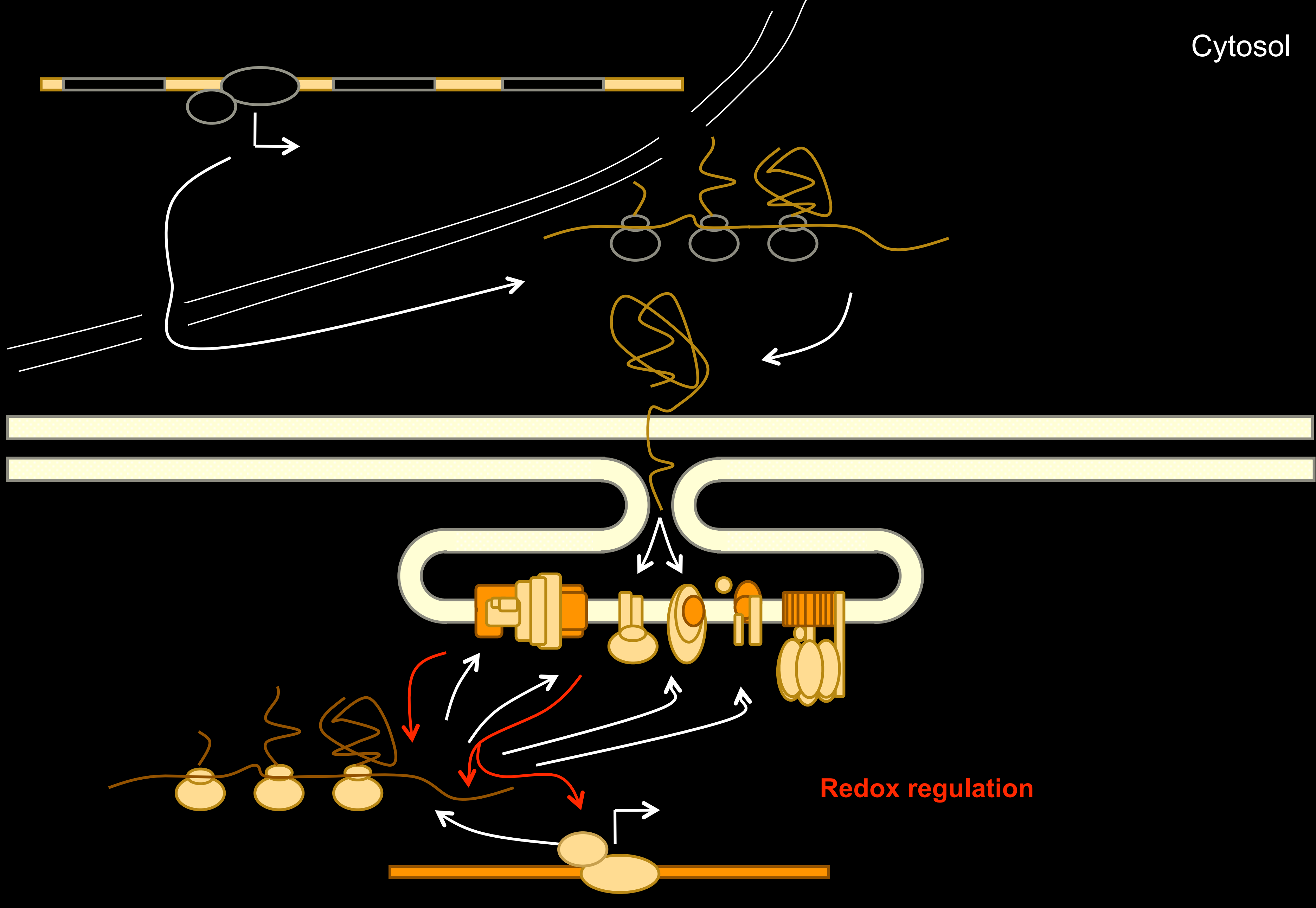


Bioenergetic organelle

Allen JF (1993) Control of Gene Expression by Redox Potential and the Requirement for Chloroplast and Mitochondrial Genomes. *Journal of Theoretical Biology* 165: 609-631




Cytosol
Mitochondrial matrix


Cytosol
Redox regulation
Mitochondrial matrix

Why mitochondria and chloroplasts have genomes

Why mitochondria and chloroplasts have genomes

Problem: Why are there genes in mitochondria and chloroplasts?

Why mitochondria and chloroplasts have genomes

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Proposed solution (hypothesis): The location has an advantage, since energy conversion, in order to be both safe and efficient, requires a set of proteins whose genes reside with them, in the same compartment of the cell.

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CoRR - **Co**-Location for **R**edox* **R**egulation.

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CoRR - **Co**-Location for **R**edox* **R**egulation.

CoRR applies equally to mitochondria and chloroplasts

*Redox reactions are chemical reaction in which an electron is transferred from one molecule to another - the basis of biological energy conversion.

CoRR

Co-Location (of gene and gene product) for **R**edox **R**egulation

CoRR

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Predictions of the **CoRR** hypothesis include:

CoRR

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CoRR

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CoRR

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4. When mitochondria and chloroplasts lose their function in energy conversion, they also lose their genomes

CoRR

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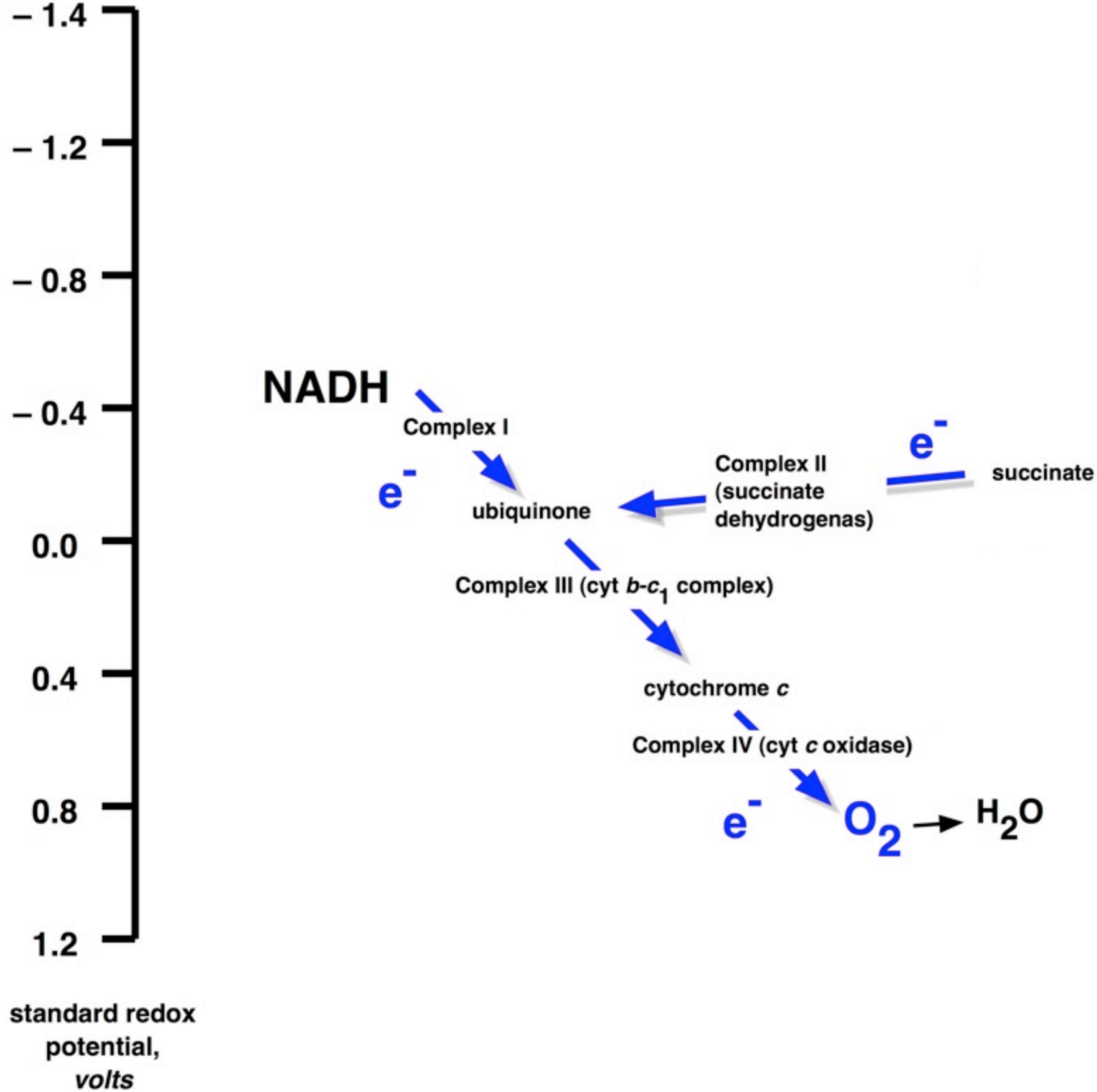
5.....

Co-location for Redox Regulation - CoRR

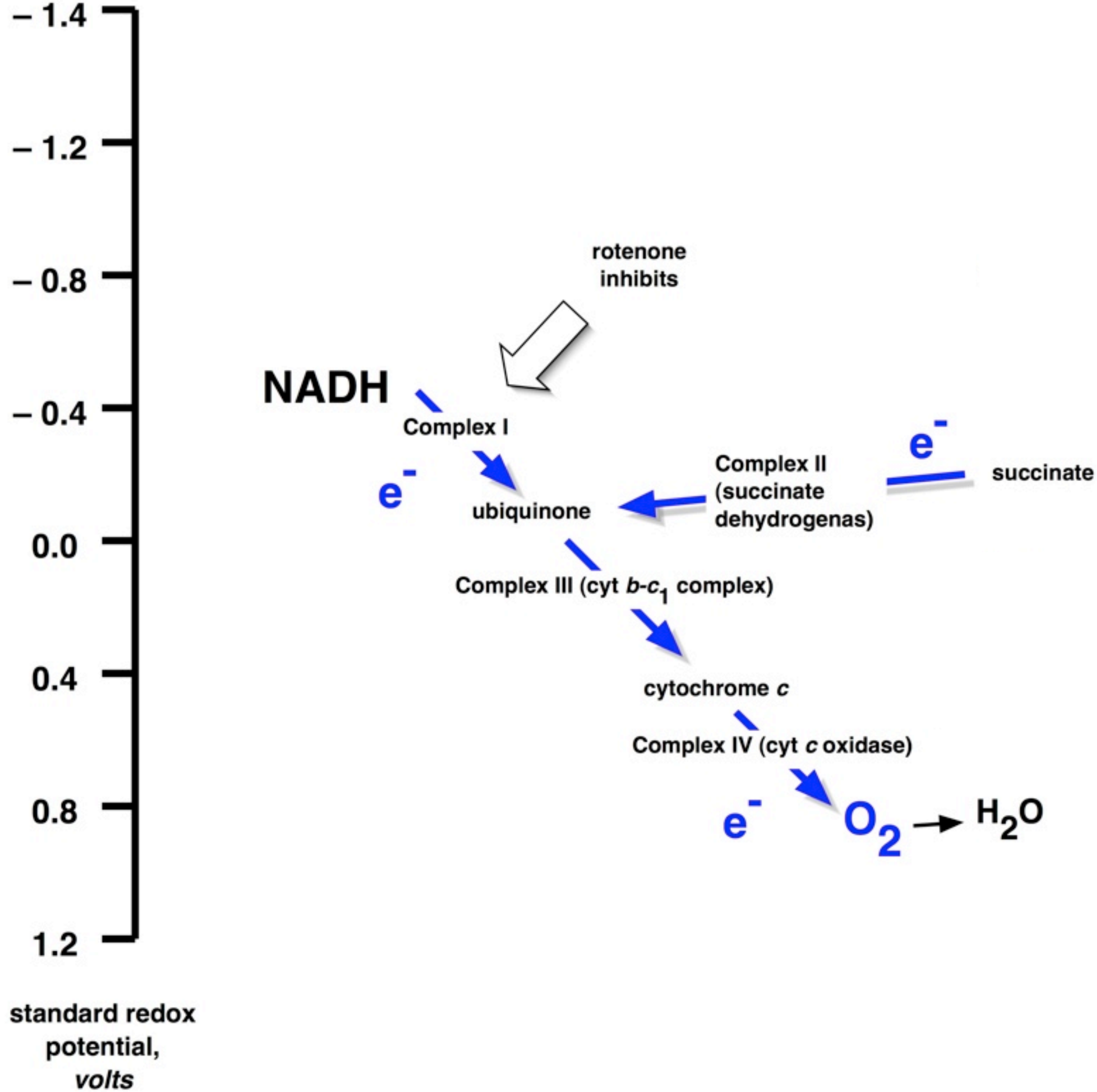
Prediction

Experimental results

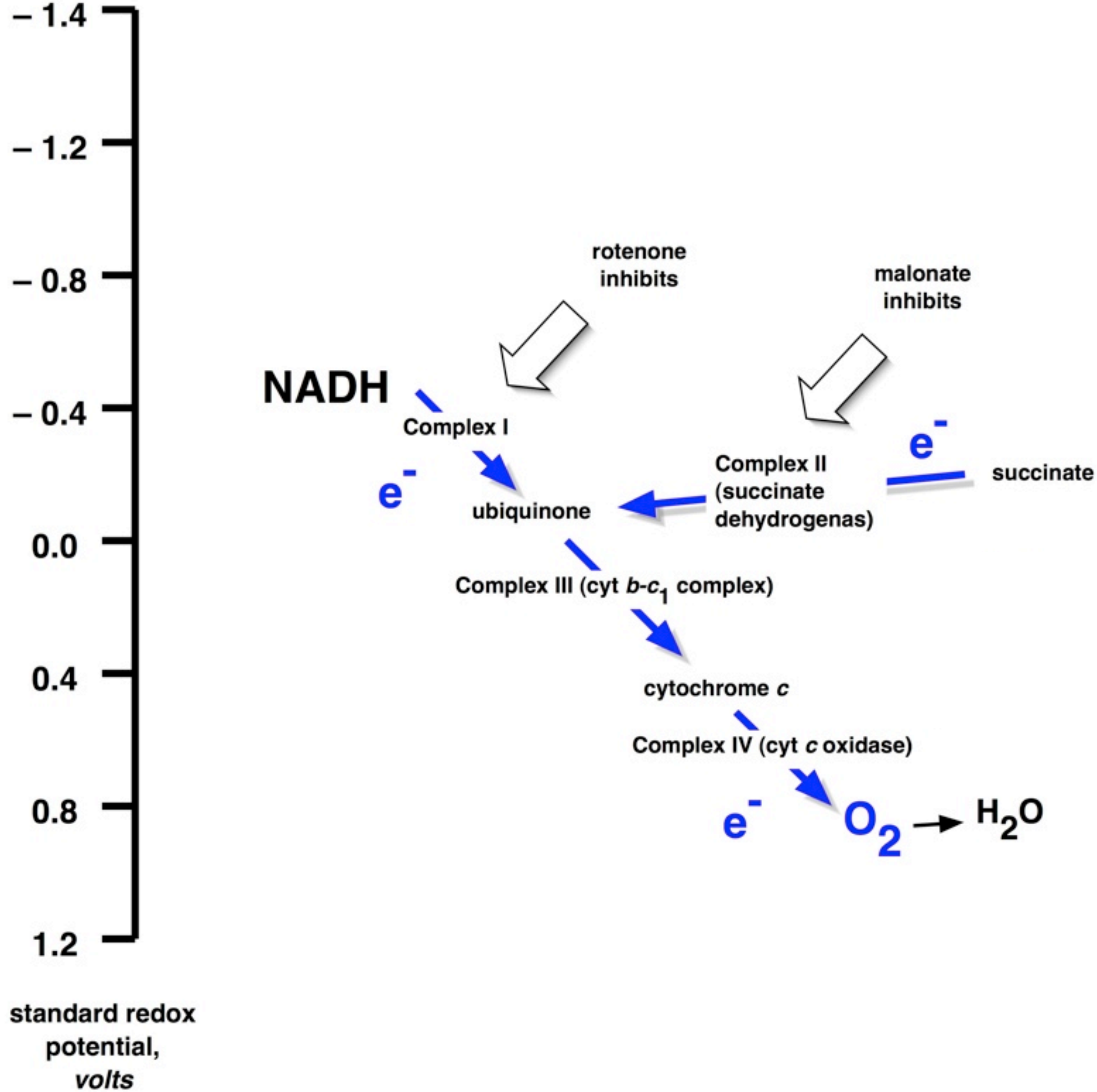
Redox regulatory control of mitochondrial and chloroplast gene expression



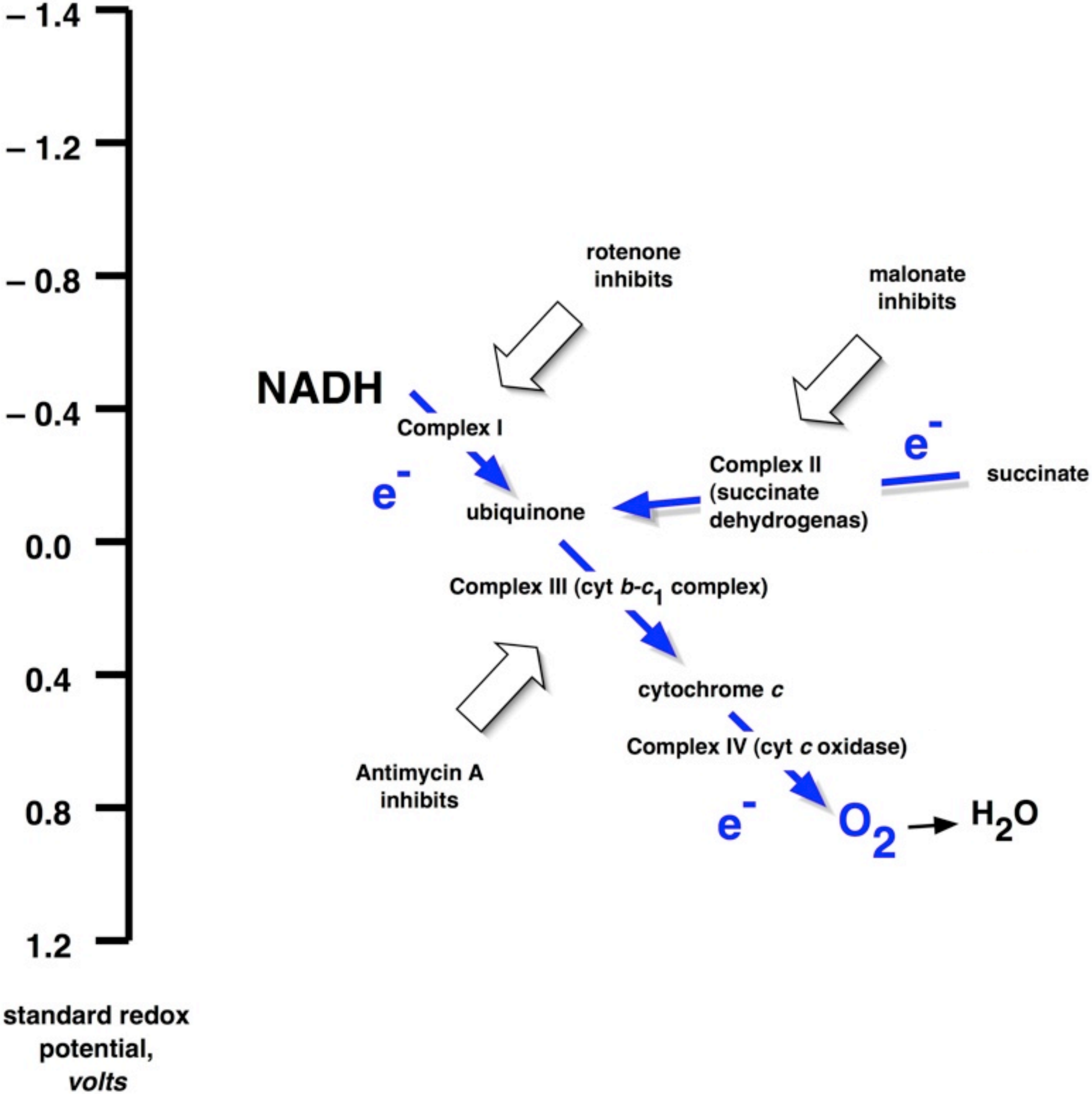
– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox potential, *volts*
NADH
Complex I
e-
ubiquinone
Complex II (succinate dehydrogenas)
e-
succinate
Complex III (cyt b-c_1 complex)
cytochrome c
Complex IV (cyt c oxidase)
e-
O_2
H_2O



– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox potential, *volts*
rotenone inhibits
NADH
Complex I
e-
ubiquinone
Complex II (succinate dehydrogenas)
e-
succinate
Complex III (cyt *b*-c_1 complex)
cytochrome *c*
Complex IV (cyt *c* oxidase)
e-
O_2
H_2O



– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox potential, *volts*
rotenone inhibits
malonate inhibits
NADH
Complex I
e-
ubiquinone
Complex II (succinate dehydrogenas)
e-
succinate
Complex III (cyt *b*-c_1 complex)
cytochrome *c*
Complex IV (cyt *c* oxidase)
e-
O_2
H_2O



– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
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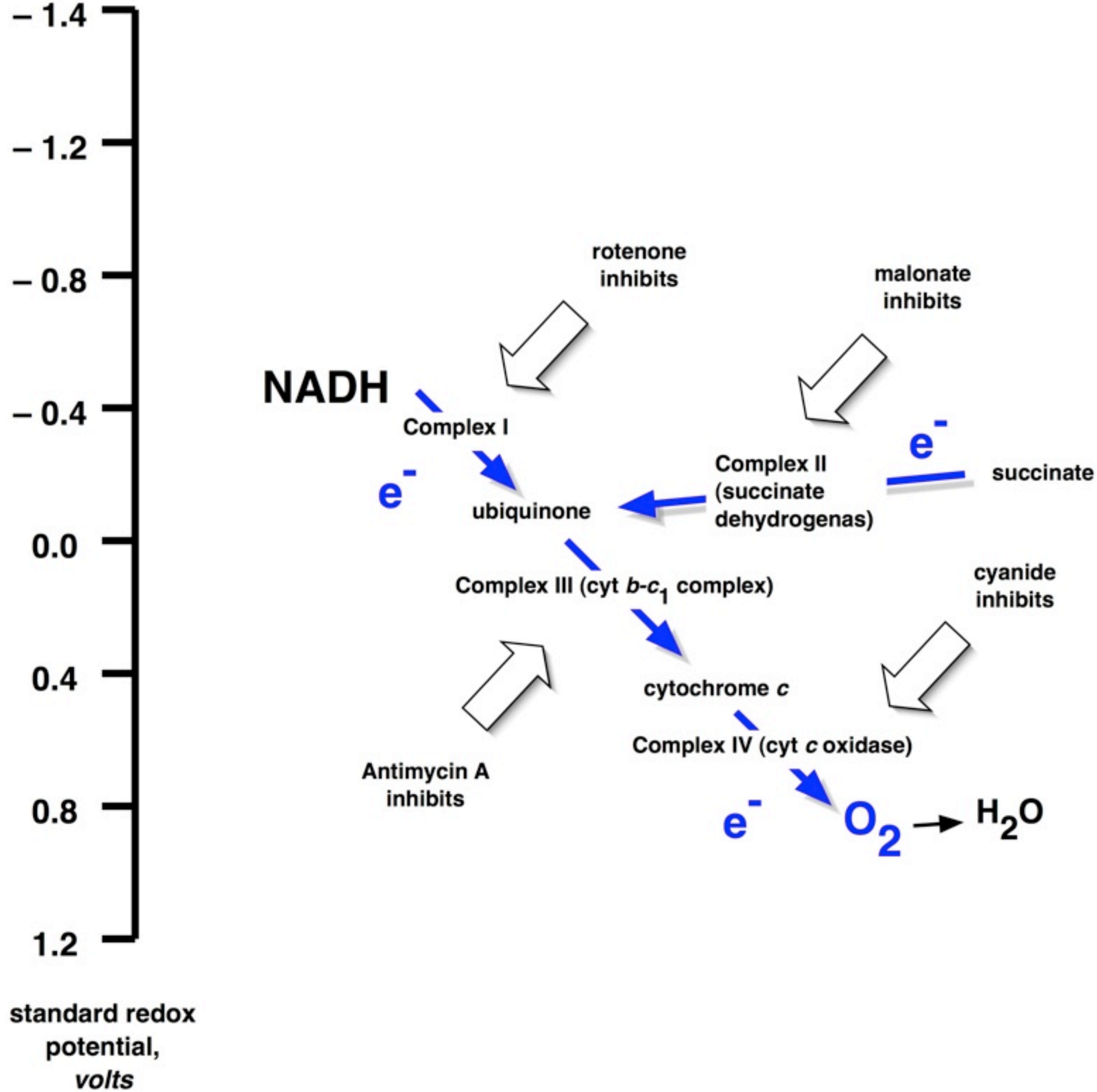
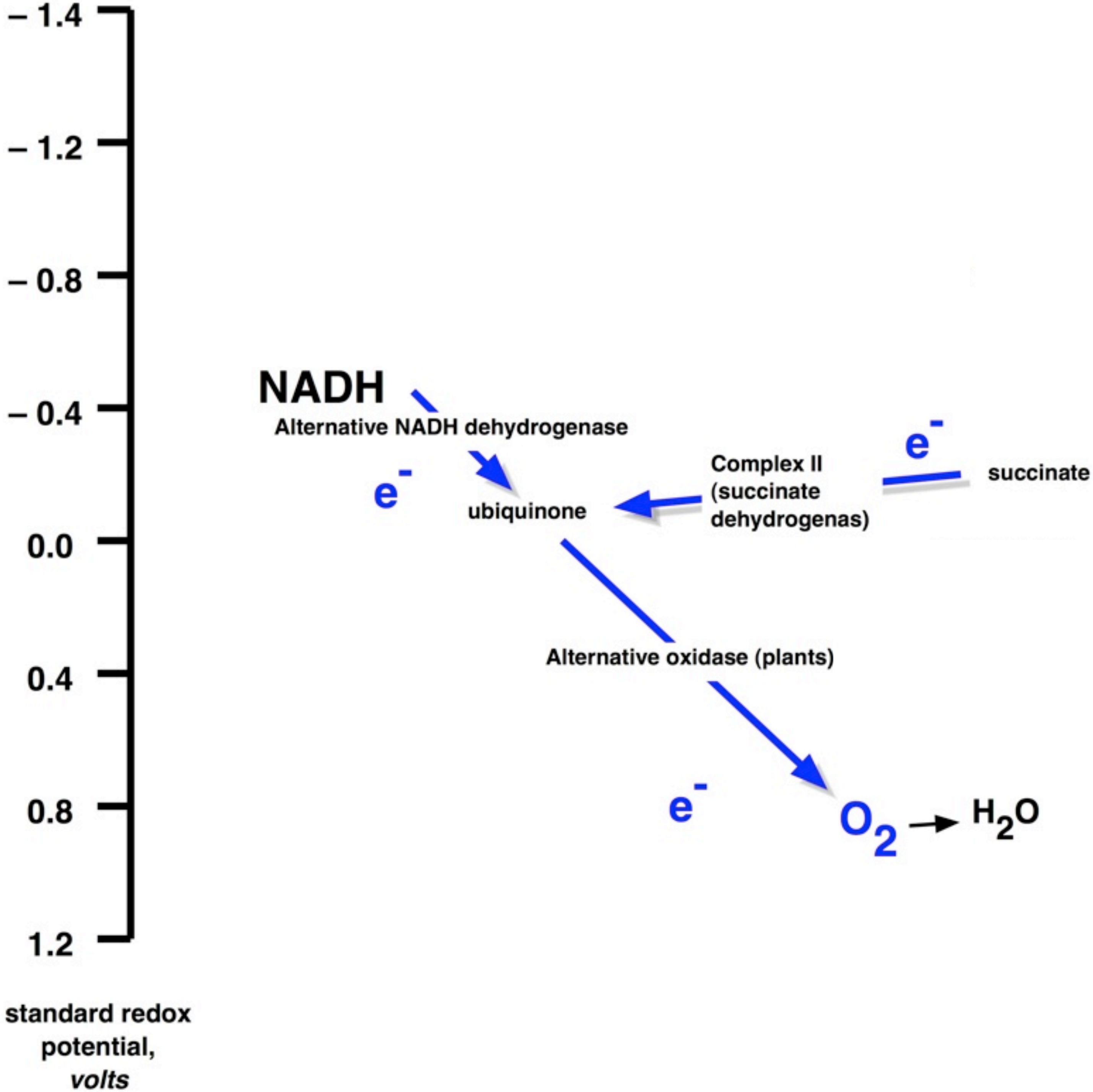
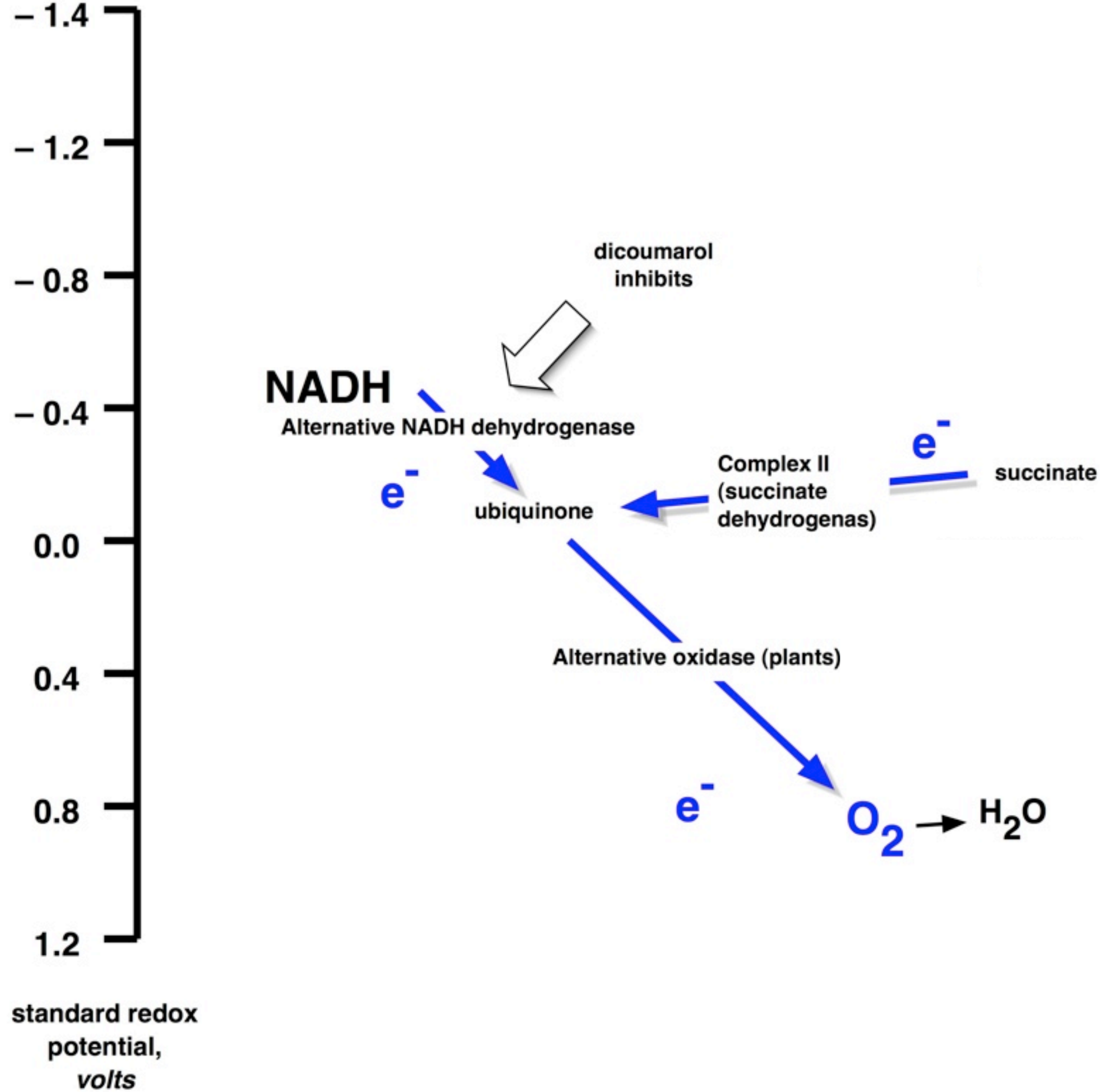
standard redox potential, *volts*
rotenone inhibits
malonate inhibits
NADH
Complex I
e-
ubiquinone
e-
Complex II (succinate dehydrogenas)
succinate
Complex III (cyt *b*-c_1 complex)
cytochrome *c*
Complex IV (cyt *c* oxidase)
Antimycin A inhibits
e-
O_2
H_2O



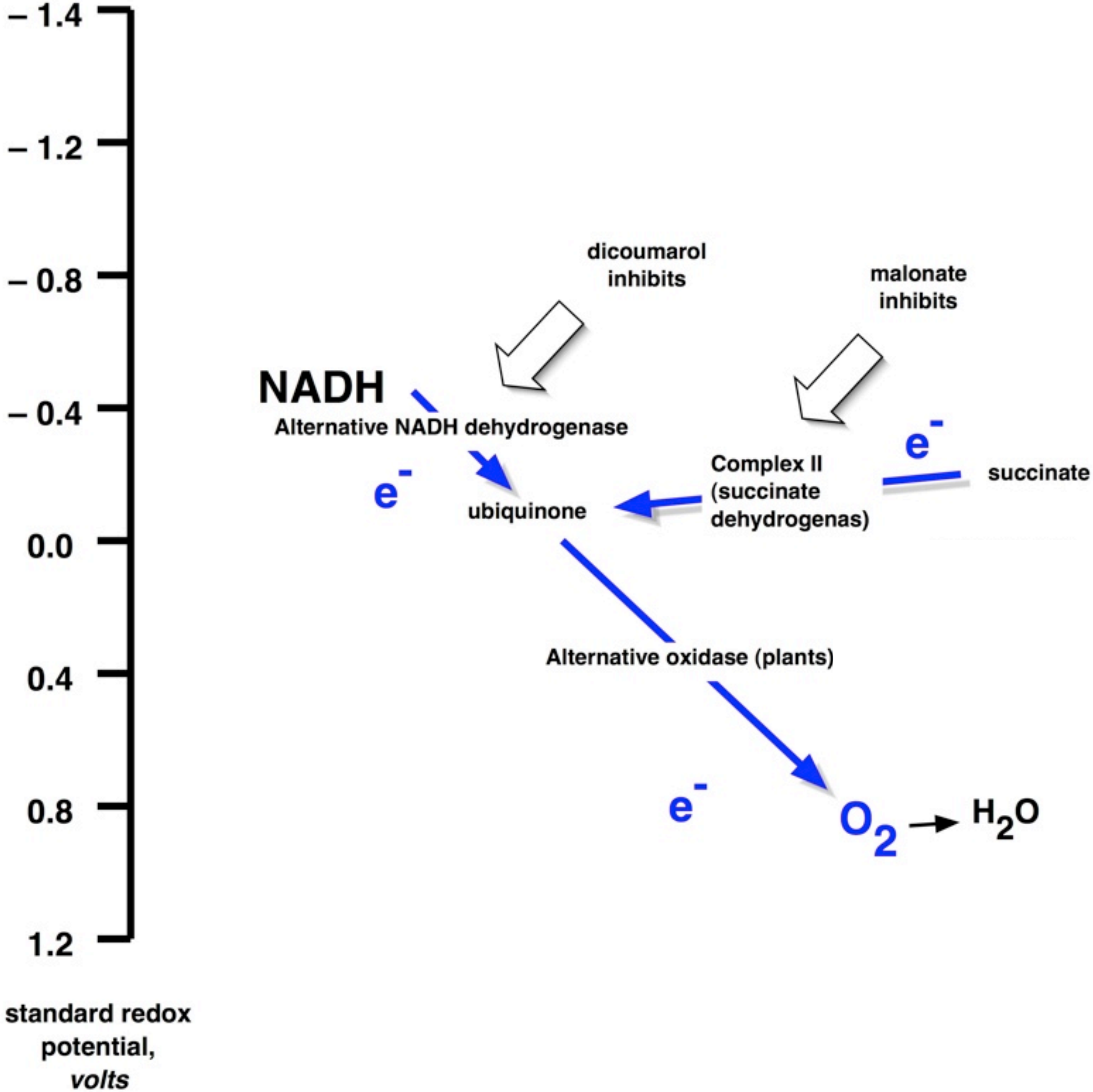
– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox potential, volts
rotenone inhibits
malonate inhibits
NADH
Complex I
e-
ubiquinone
Complex II (succinate dehydrogenas)
e-
succinate
Complex III (cyt b-c1 complex)
cyanide inhibits
cytochrome c
Complex IV (cyt c oxidase)
Antimycin A inhibits
e-
O2
H2O



– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox potential, *volts*
NADH
Alternative NADH dehydrogenase
e-
ubiquinone
Complex II (succinate dehydrogenas)
e-
succinate
Alternative oxidase (plants)
e-
O_2 → H_2O



– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox
potential,
volts
dicoumarol
inhibits
NADH
Alternative NADH dehydrogenase
e-
ubiquinone
Complex II
(succinate
dehydrogenas)
e-
succinate
Alternative oxidase (plants)
e-
O_2 → H_2O



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dicoumarol inhibits
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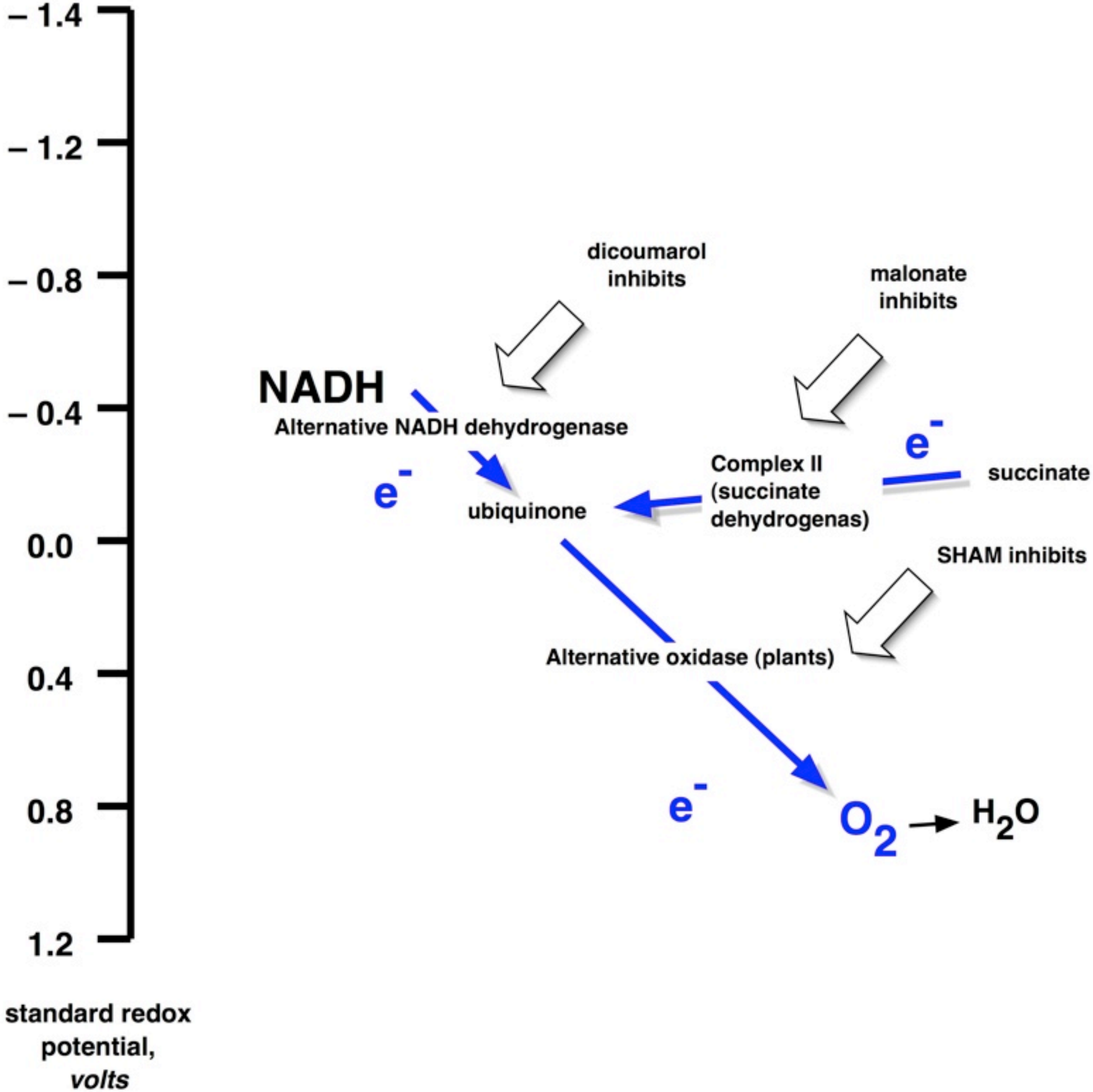
NADH
Alternative NADH dehydrogenase
e^-
ubiquinone
Complex II (succinate dehydrogenas)
e^-
succinate
Alternative oxidase (plants)
e^-
O_2
H_2O



– 1.4
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0.0
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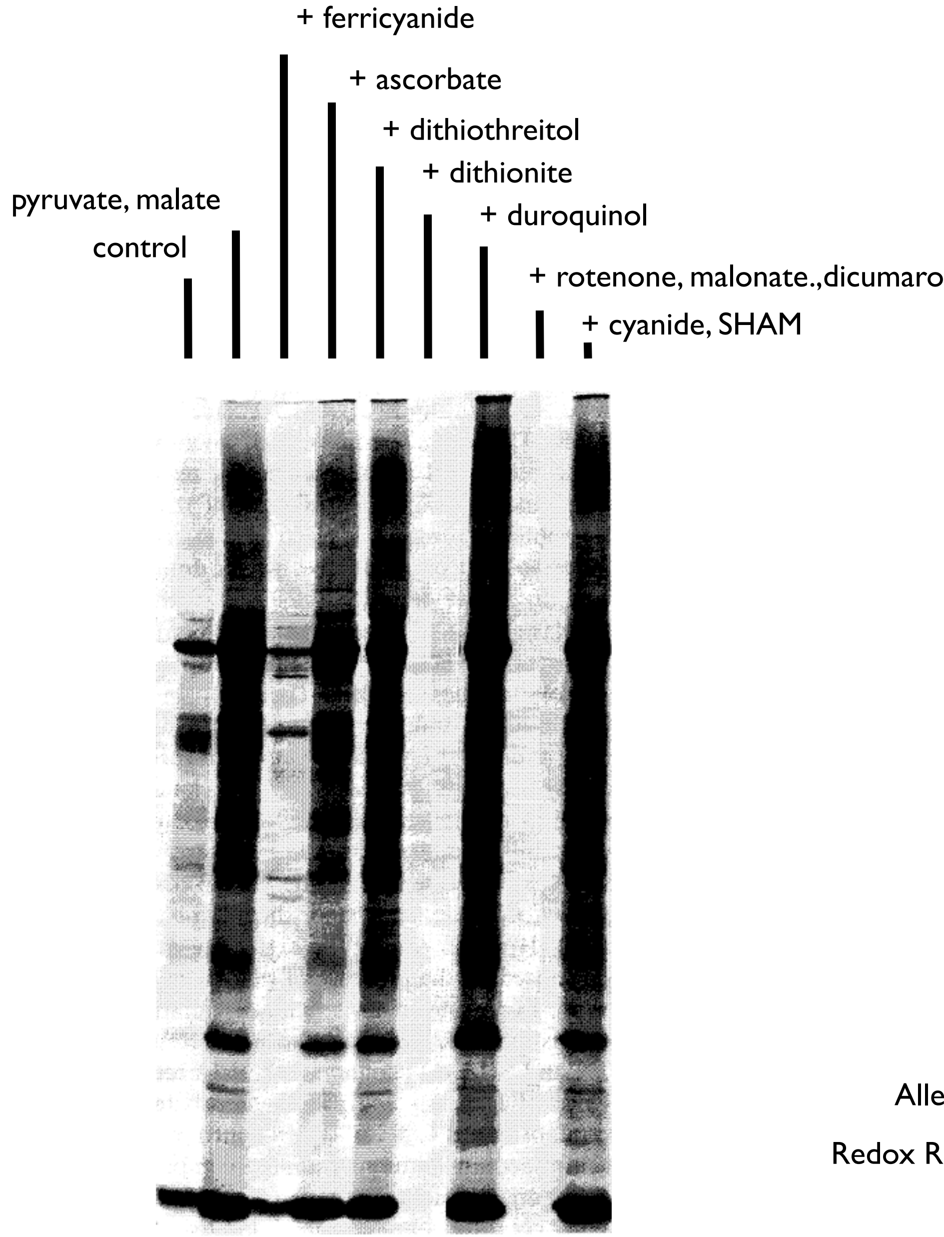
standard redox potential, *volts*
dicoumarol inhibits
malonate inhibits
NADH
Alternative NADH dehydrogenase
e-
e-
Complex II (succinate dehydrogenas)
succinate
ubiquinone
SHAM inhibits
Alternative oxidase (plants)
e-
O_2 → H_2O



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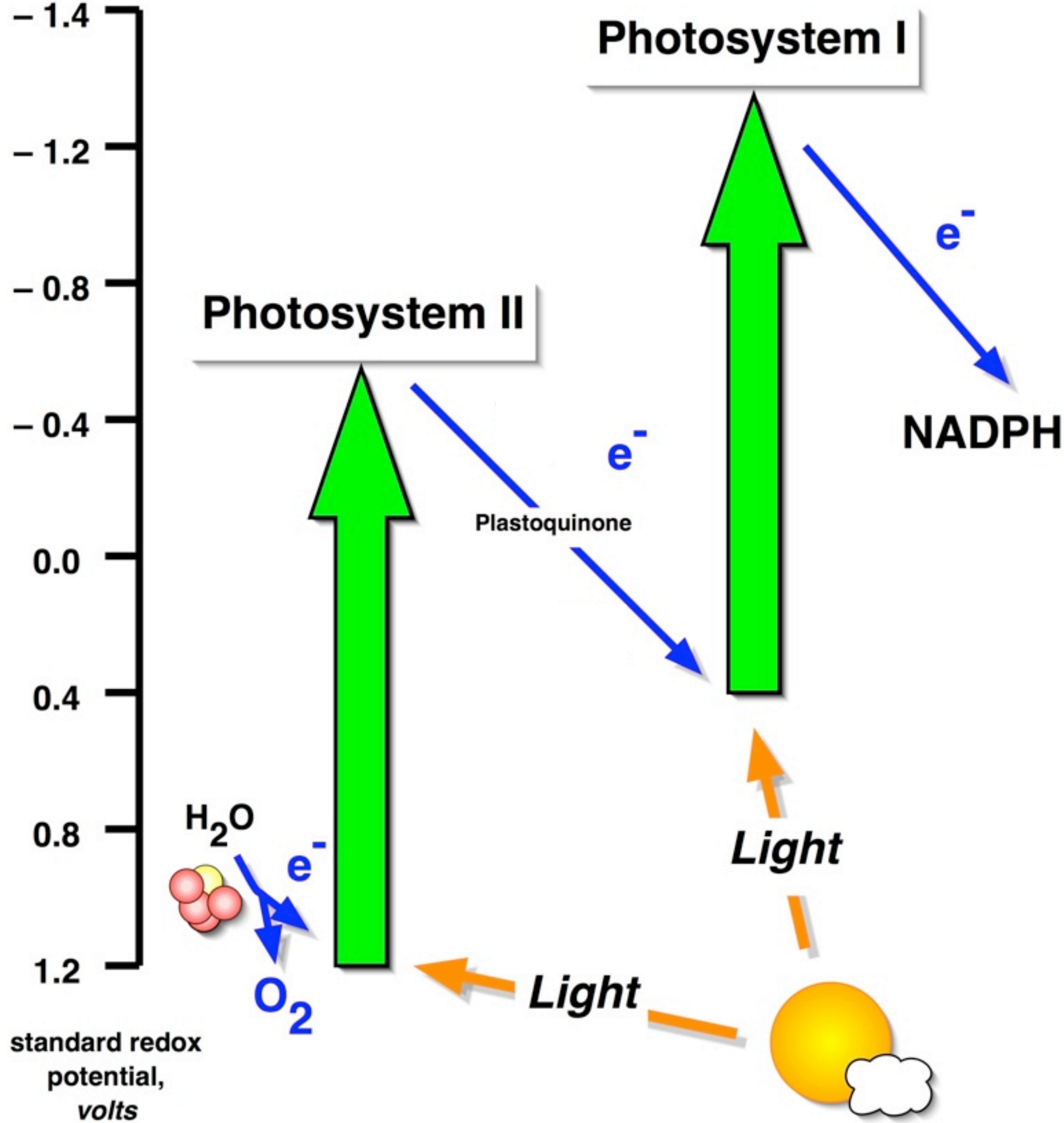
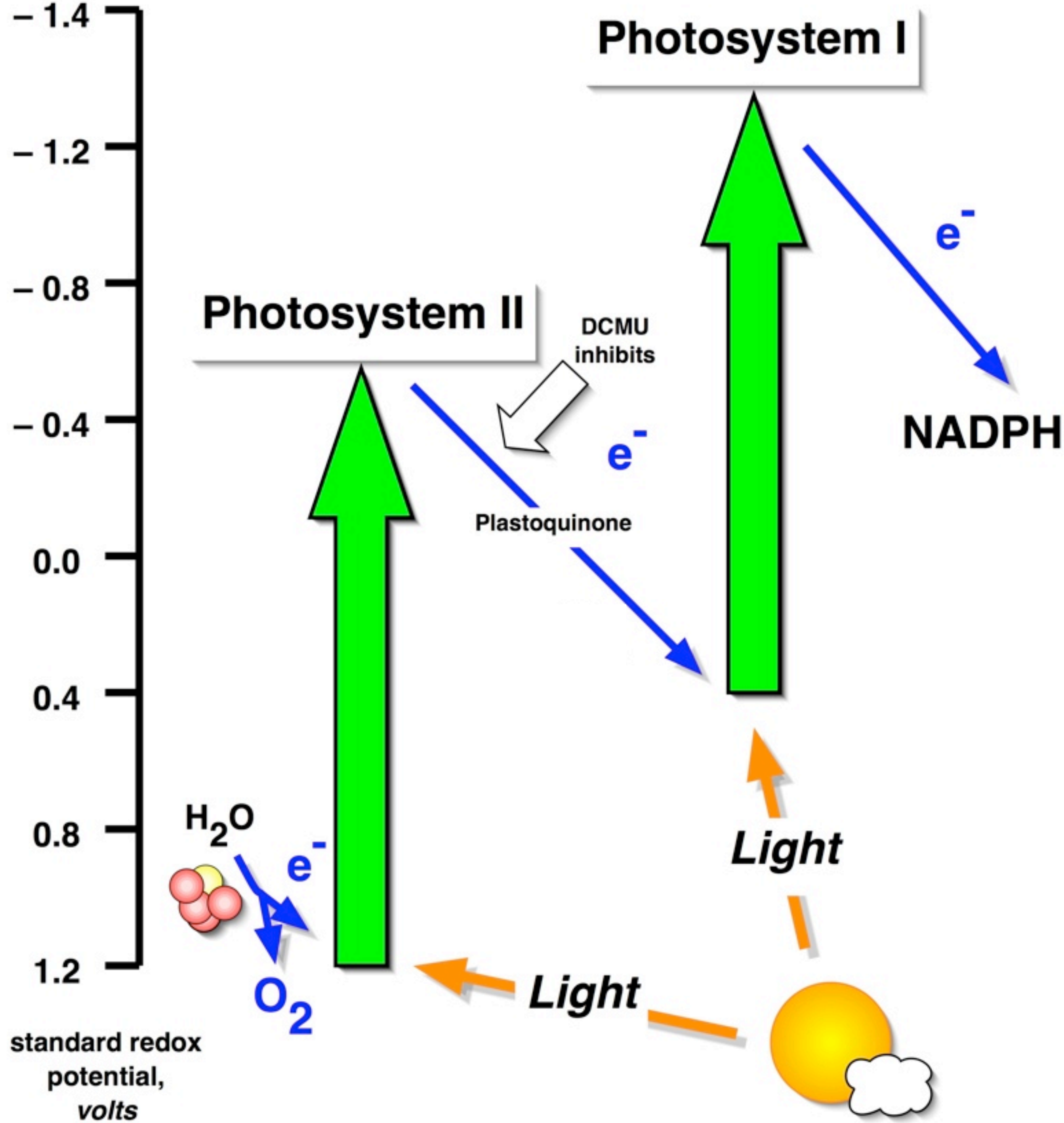
Redox Report 1, 119-123

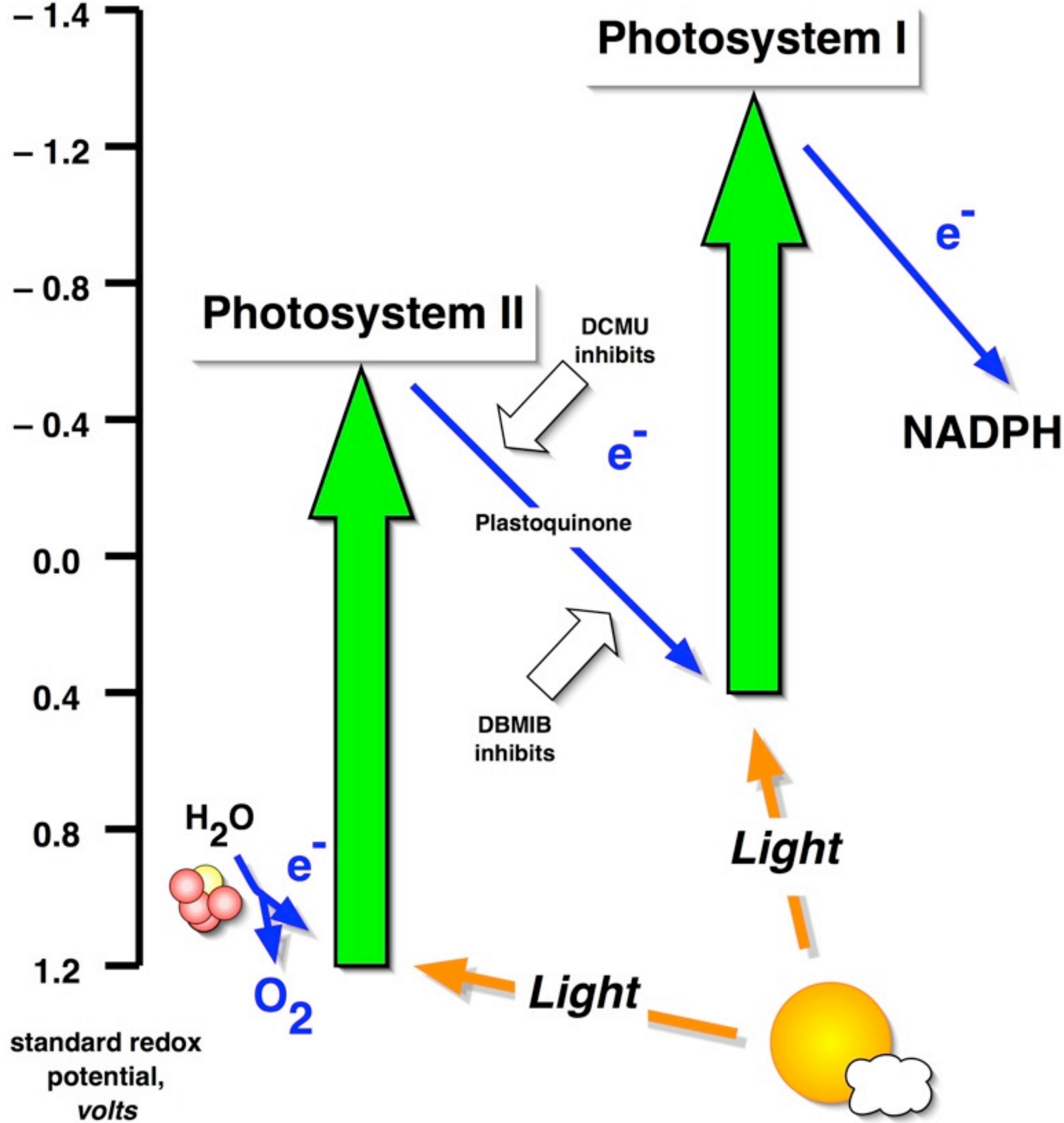
^{35}S-methionine labelling of newly synthesised proteins in pea leaf mitochondria



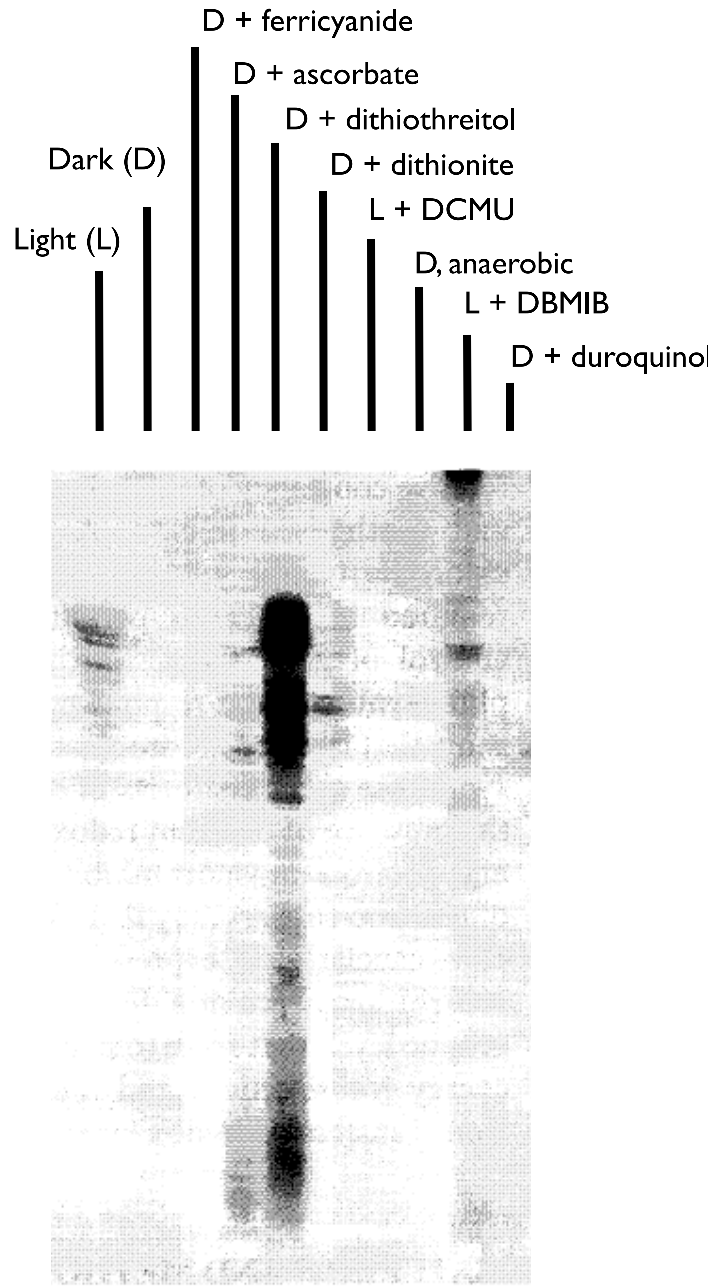
– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox potential, *volts*
Photosystem I
Photosystem II
e-
e-
e-
NADPH
Plastoquinone
H2O
O2
Light
Light



– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox potential, *volts*
Photosystem I
Photosystem II
DCMU inhibits
e-
Plastoquinone
NADPH
H_2O
O_2
Light
Light



– 1.4
– 1.2
– 0.8
– 0.4
0.0
0.4
0.8
1.2
standard redox potential, *volts*
Photosystem I
Photosystem II
DCMU inhibits
DBMIB inhibits
Plastoquinone
e-
e-
e-
NADPH
H_2O
O_2
Light
Light



Allen, C. A. et al

Redox Report 1, 119-123

^{35}S-methionine labelling of newly synthesised proteins in pea leaf chloroplast stroma

Co-location for **R**edox **R**egulation - **CoRR**

Prediction

Experimental results

Redox regulatory control of chloroplast and mitochondrial transcription


31. 7. 2001


31. 7. 2001

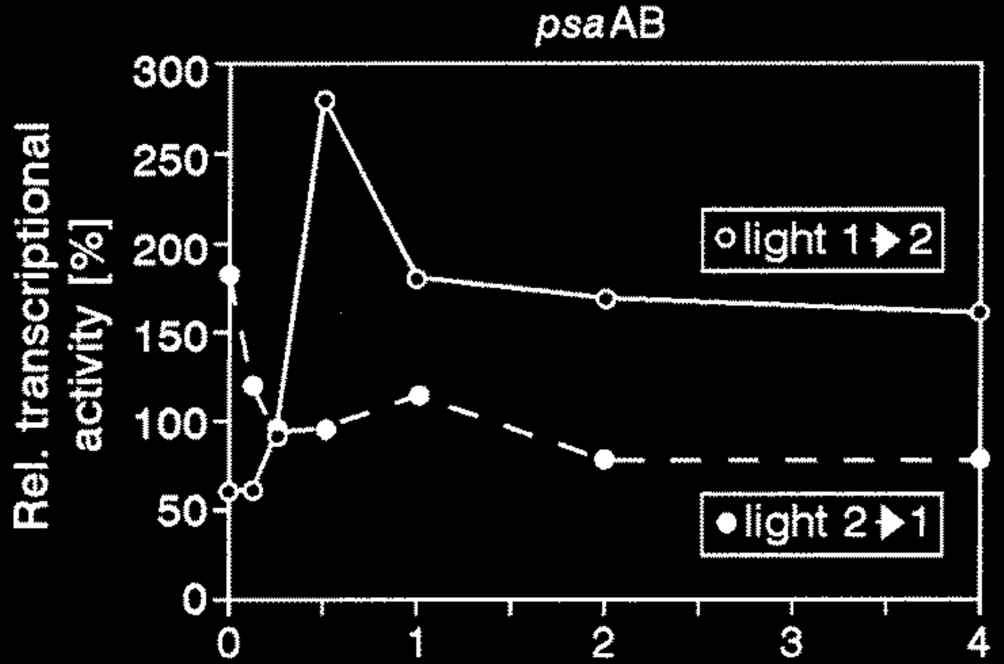

31. 7. 2001


Light I
31. 7. 2001

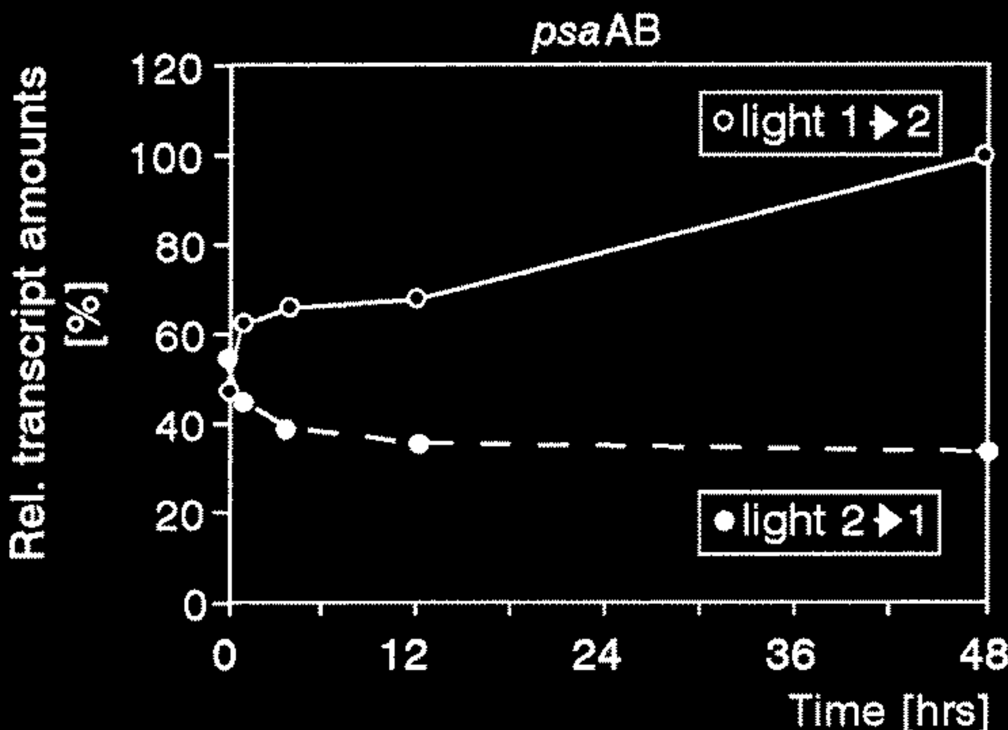

31. 7. 2001


Light 1
31. 7. 2001

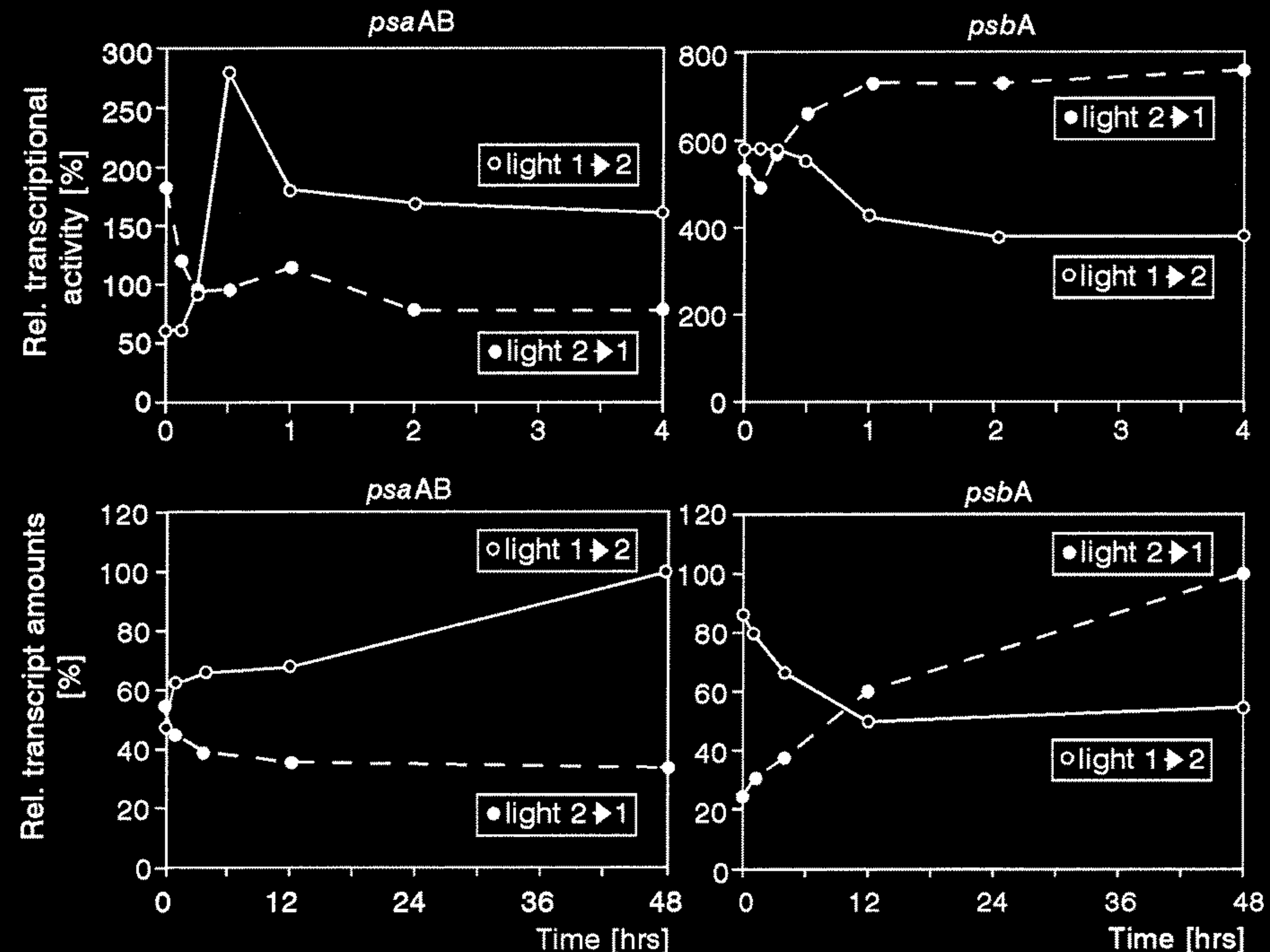

Light 2
31. 7. 2001



psaAB
Rel. transcriptional activity [%]
300
250
200
150
100
50
0
light 1 ▶ 2
light 2 ▶ 1
0
1
2
3
4



psaAB
Rel. transcript amounts [%]
120
100
80
60
40
20
0
light 1 ▶ 2
light 2 ▶ 1
0
12
24
36
48
Time [hrs]


psaAB
psbA
Rel. transcriptional activity [%]
300
250
200
150
100
50
0
800
600
400
200
0
light 1 ▶ 2
light 2 ▶ 1
0
1
2
3
4
psaAB
psbA
Rel. transcript amounts [%]
120
100
80
60
40
20
0
0
12
24
36
48
Time [hrs]
Time [hrs]

Co-location for **R**edox **R**egulation - **CoRR**

Prediction

Experimental results

Persistence of "bacterial" redox signalling components
in chloroplasts and mitochondria

The ancestral symbiont sensor kinase CSK links photosynthesis with gene expression in chloroplasts

Sujith Puthiyaveetil*, T. Anthony Kavanagh†, Peter Cain‡, James A. Sullivan*, Christine A. Newell§, John C. Gray§, Colin Robinson‡, Mark van der Giezen¶, Matthew B. Rogers¶, and John F. Allen*‖

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Communicated by Elisabeth Gantt, University of Maryland, College Park, MD, April 25, 2008 (received for review February 15, 2008)

We describe a novel, typically prokaryotic, sensor kinase in chloroplasts of green plants. The gene for this chloroplast sensor kinase (CSK) is found in cyanobacteria, prokaryotes from which chloroplasts evolved. The CSK gene has moved, during evolution, from the ancestral chloroplast to the nuclear genomes of eukaryotic algae and green plants. The CSK protein is now synthesised in the cytosol of photosynthetic eukaryotes and imported into their chloroplasts as a protein precursor. In the model higher plant *Arabidopsis thaliana*, CSK is autophosphorylated and required for control of transcription of chloroplast genes by the redox state of an electron carrier connecting photosystems I and II. CSK therefore provides a redox regulatory mechanism that couples photosynthesis to gene expression. This mechanism is inherited directly from the cyanobacterial ancestor of chloroplasts, is intrinsic to chloroplasts, and is targeted to chloroplast genes.

limited to a few examples in certain nongreen algal groups, where there are just one or two two-component genes of uncertain function in the chloroplast genome itself (8).

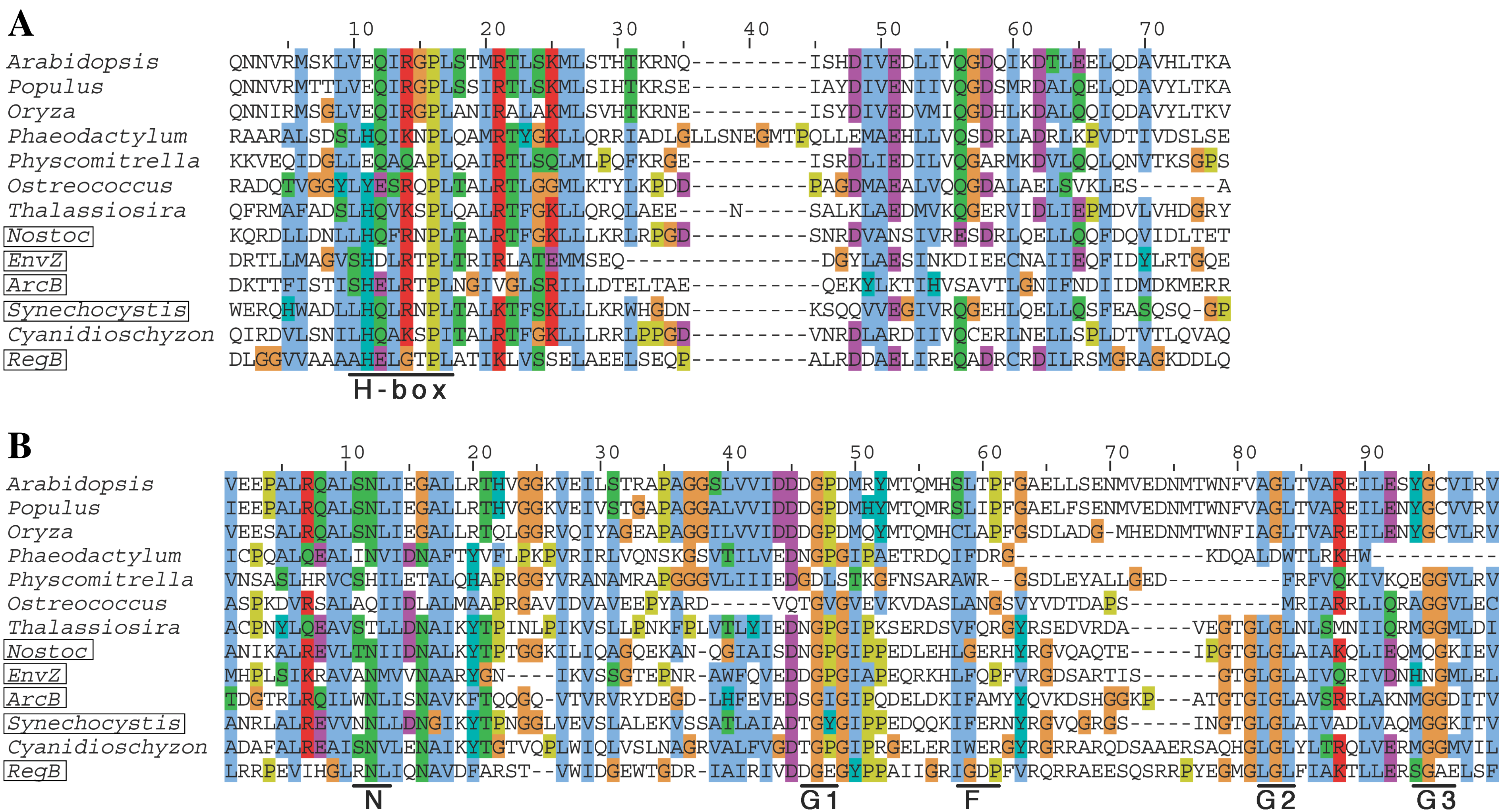
Author contributions: S.P. and J.F.A. designed research; S.P., T.A.K., P.C., C.A.N., and J.F.A. performed research; S.P., T.A.K., J.A.S., and M.v.d.G. contributed new reagents/analytic tools; S.P., T.A.K., P.C., J.C.G., C.R., M.v.d.G., M.B.R., and J.F.A. analyzed data; and S.P. and J.F.A. wrote the paper.

The authors declare no conflict of interest.

Freely available online through the PNAS open access option.

‖To whom correspondence should be addressed. E-mail: j.f.allen@qmul.ac.uk.

This article contains supporting information online at www.pnas.org/cgi/content/full/0803928105/DCSupplemental.



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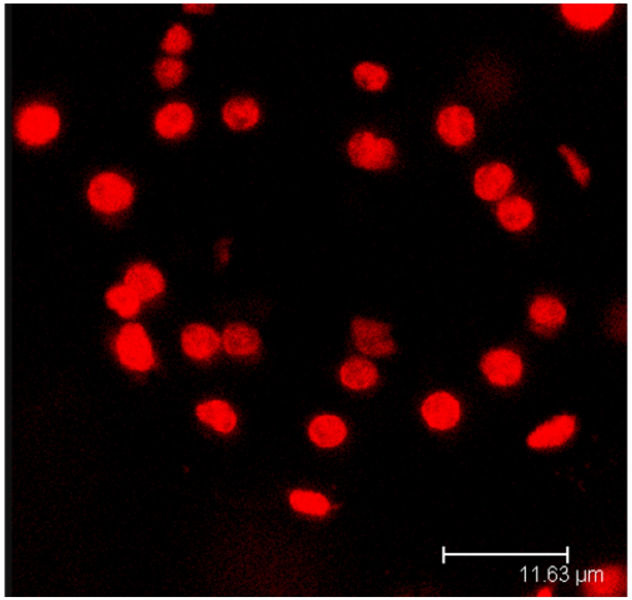

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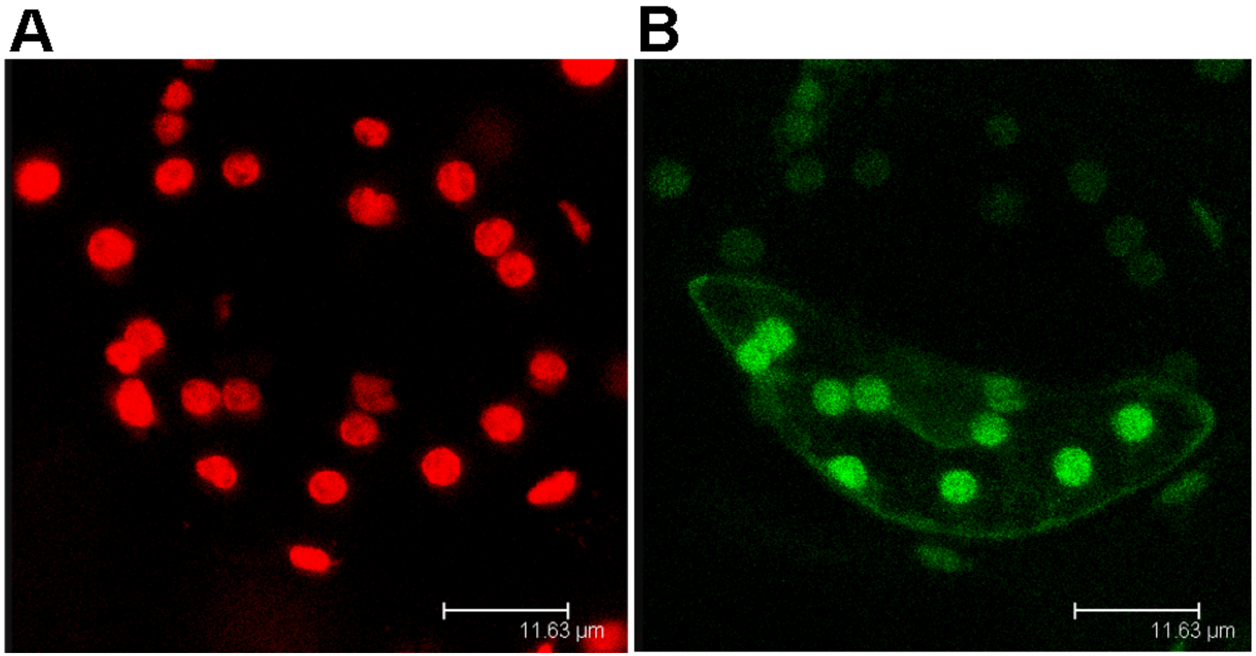

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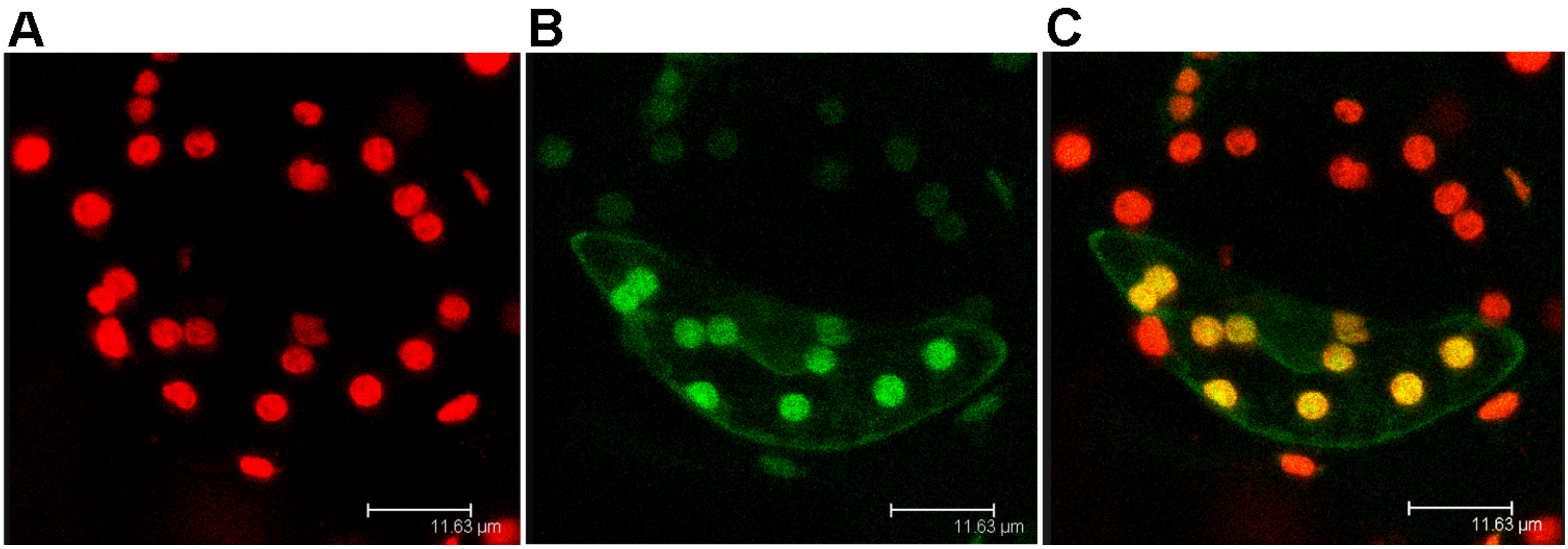

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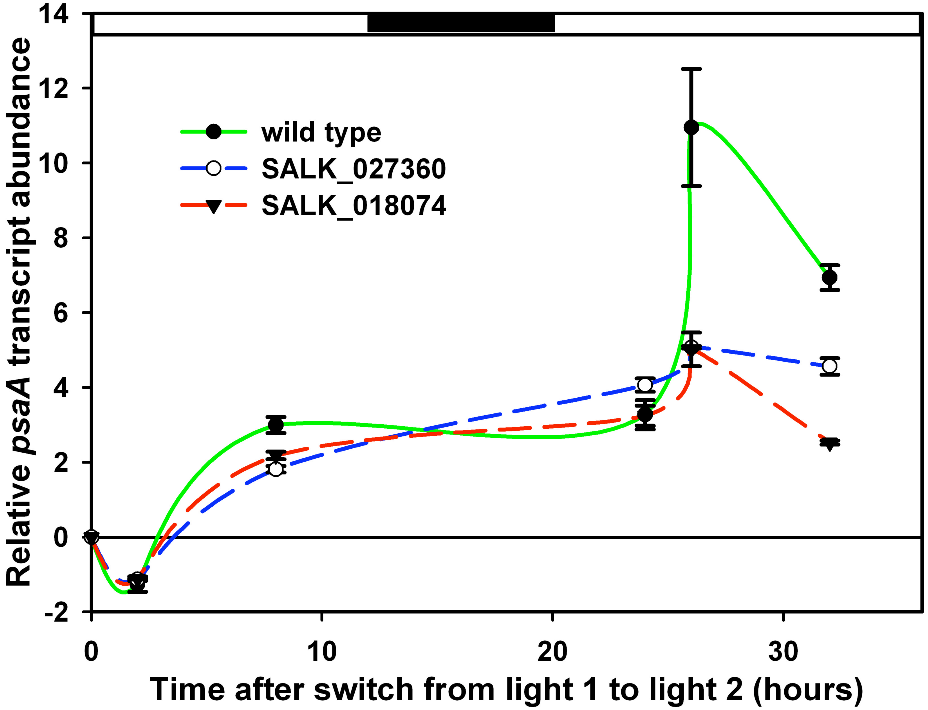

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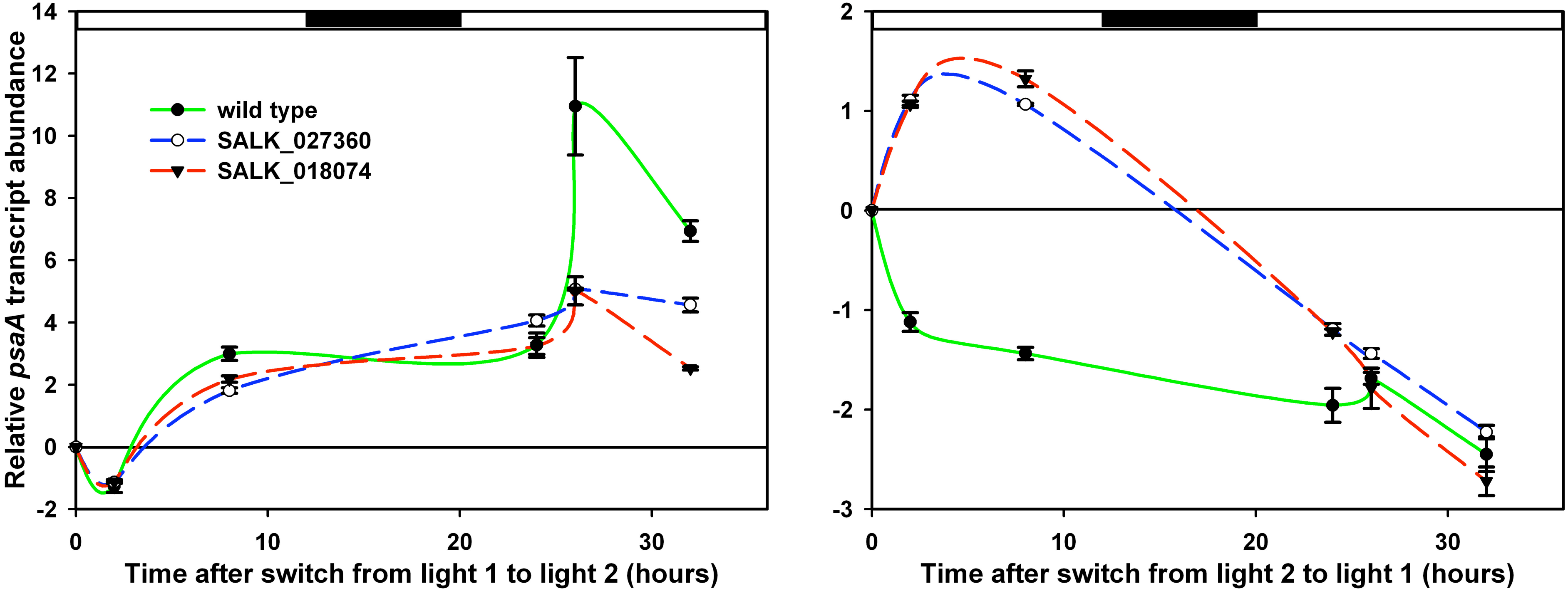

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CSK

- **C**hloroplast **S**ensor **K**inase
- A Histidine sensor kinase homologous with Hik2 of cyanobacteria
- A *Redox Sensor*
- Sujith Puthiyaveetil

Costs of DNA in mitochondria

Why Do We Still Have a Maternally Inherited Mitochondrial DNA? Insights from Evolutionary Medicine

Douglas C. Wallace

Center for Molecular and Mitochondrial Medicine and Genetics, Departments of Biological Chemistry, Ecology and Evolutionary Biology, and Pediatrics, University of California, Irvine, California 92697-3940; email: dwallace@uci.edu

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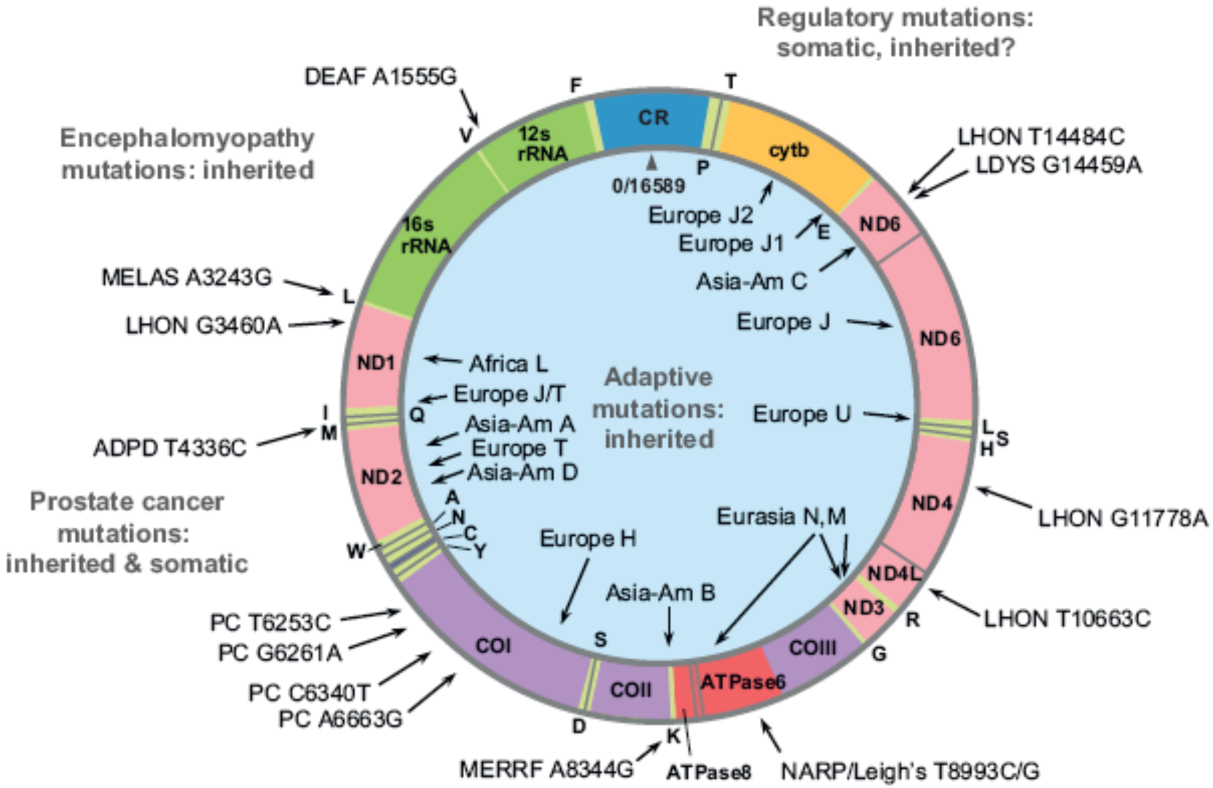
0066-4154/07/0707-0781$20.00

Key Words

adaptation, genomic evolution, mitochondrial disease, mtDNA, oxidative phosphorylation, proton-translocating OXPHOS complexes

Abstract

The human cell is a symbiosis of two life forms, the nucleus-cytosol and the mitochondrion. The nucleus-cytosol emphasizes structure and its genes are Mendelian, whereas the mitochondrion specializes in energy and its mitochondrial DNA (mtDNA) genes are maternal. Mitochondria oxidize calories via oxidative phosphorylation (OXPHOS) to generate a mitochondrial inner membrane proton gradient (ΔP). ΔP then acts as a source of potential energy to produce ATP, generate heat, regulate reactive oxygen species (ROS), and control apoptosis, etc. Interspecific comparisons of mtDNAs have revealed that the mtDNA retains a core set of electron and proton carrier genes for the proton-translocating OXPHOS complexes I, III, IV, and V. Human mtDNA analysis has revealed these genes frequently contain region-specific adaptive polymorphisms. Therefore, the mtDNA with its energy controlling genes may have been retained to permit rapid adaptation to new environments.



The mitochondrial genome:
mtDNA = 37 genes
Extracellular plasmids (chromosomes) ~ 1500 genes

Figure 2

The human mtDNA map. The human mtDNA encompasses three classes of clinically relevant mutations: recent maternally inherited disease-causing mutations, examples of which are shown on the outside of the circular map; ancient geographically correlated and frequently adaptive polymorphic variants, examples presented inside the circle; and somatic mutations that accumulate with age in postmitotic tissues and provide the aging clock. Letters around the outside perimeter indicate cognate amino acids of the tRNA genes. Letters within the ring represent the proteins encoded by the gene sector, all of which are integral membrane components of the proton-translocating complexes of OXPHOS. The polypeptides, corresponding gene, and complexes are ND1-4, -4L, -5, and -6 (*nad1-4*, *-4l*, *-5*, and *-6* gene) of complex I; cytb or cytochrome *b* (*cob* gene) of complex III; COI-III (*cox1–3* genes) of complex IV; and ATP6 and ATP8 (*atp6* and *atp8* genes) of complex V.


The mitochondrial
theory of ageing

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"Errors" in electron transfer - transfers to the "wrong" electron acceptor - occur at fixed frequency.

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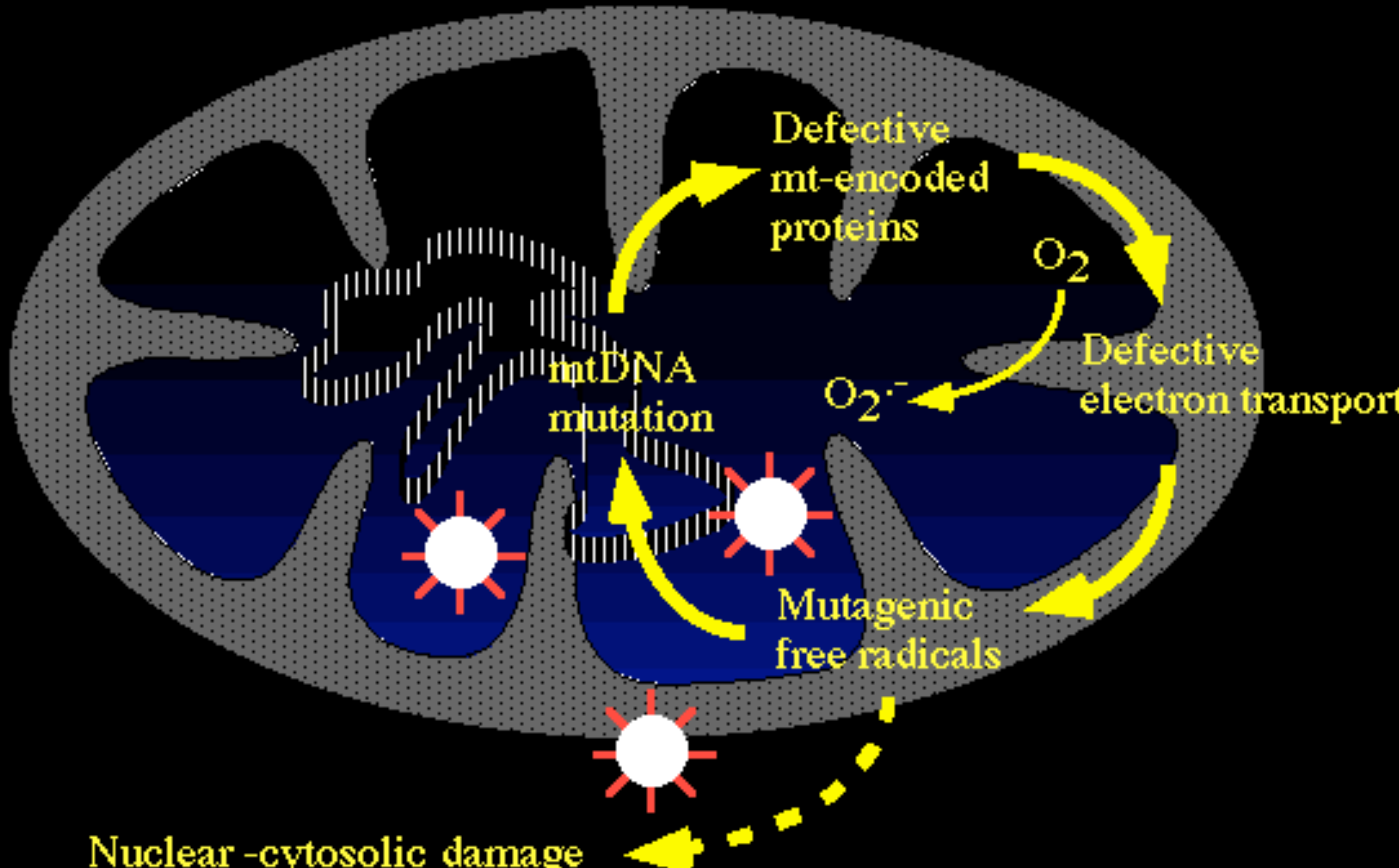
The products of these reactions damage mitochondrial genes, which then produce defective proteins, which then make more "errors" in electron transfer....damaging more genes, making more defective proteins....and so on.



Defective
mt-encoded
proteins
O_2
Defective
electron transport
$O_2^{\cdot-}$
mtDNA
mutation
Mutagenic
free radicals
Nuclear -cytosolic damage


Separate sexes as mitochondrial division of labour

Why there are two sexes

Why there are two sexes

Problem: Mitochondrial Ageing predicts that offspring should inherit their mothers' acquired state of accumulated damage, but they evidently do not. Babies are not born at the physical age of their mothers.

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Proposed solution (hypothesis): Separation of two sexes allows specialisation of mitochondria **either** as genetic templates (female germ line) **or** as energy-converters (male germ line)**.**

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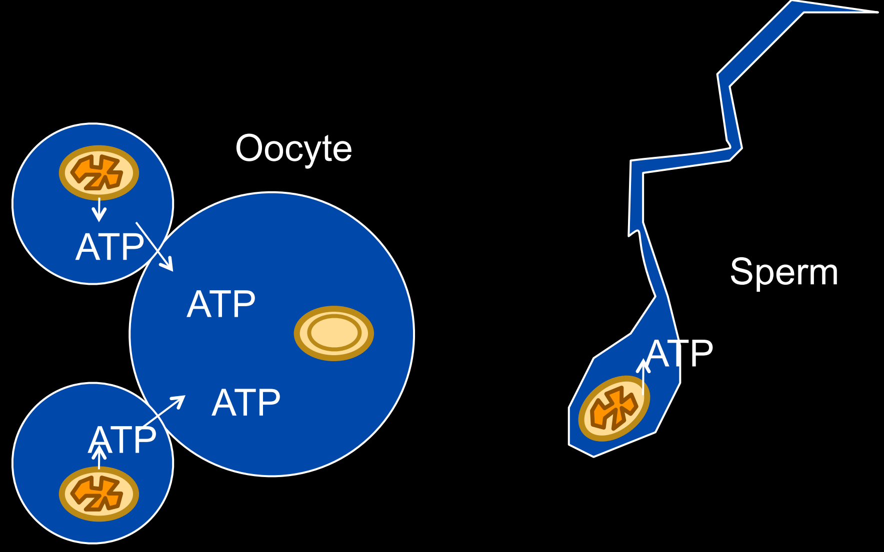
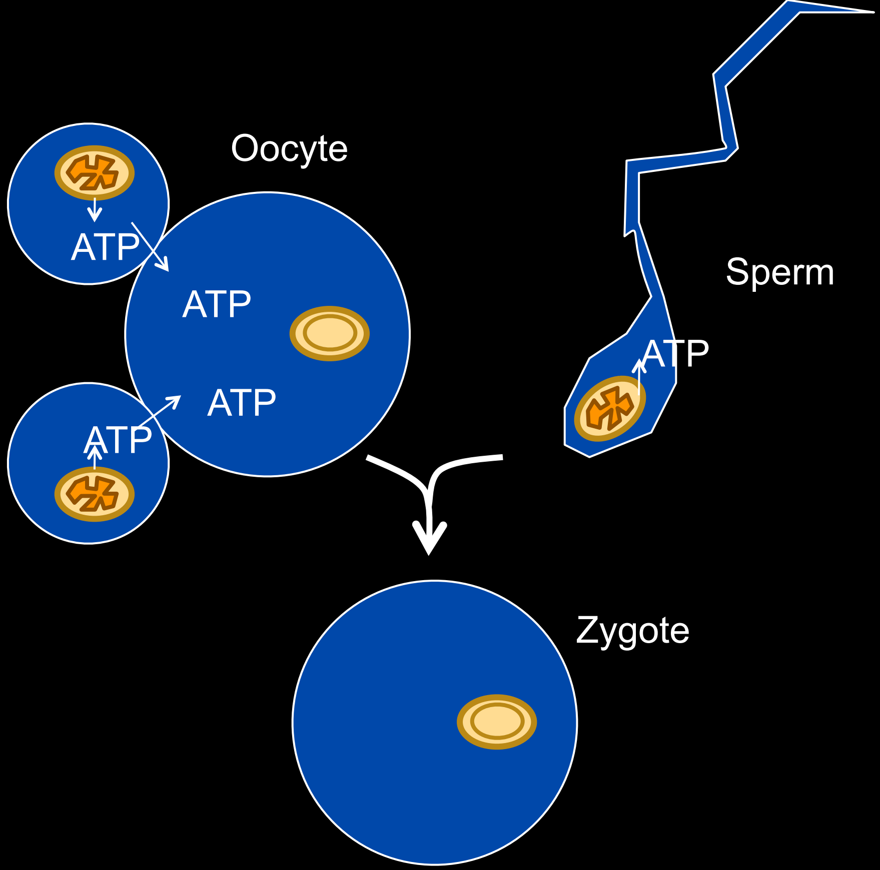
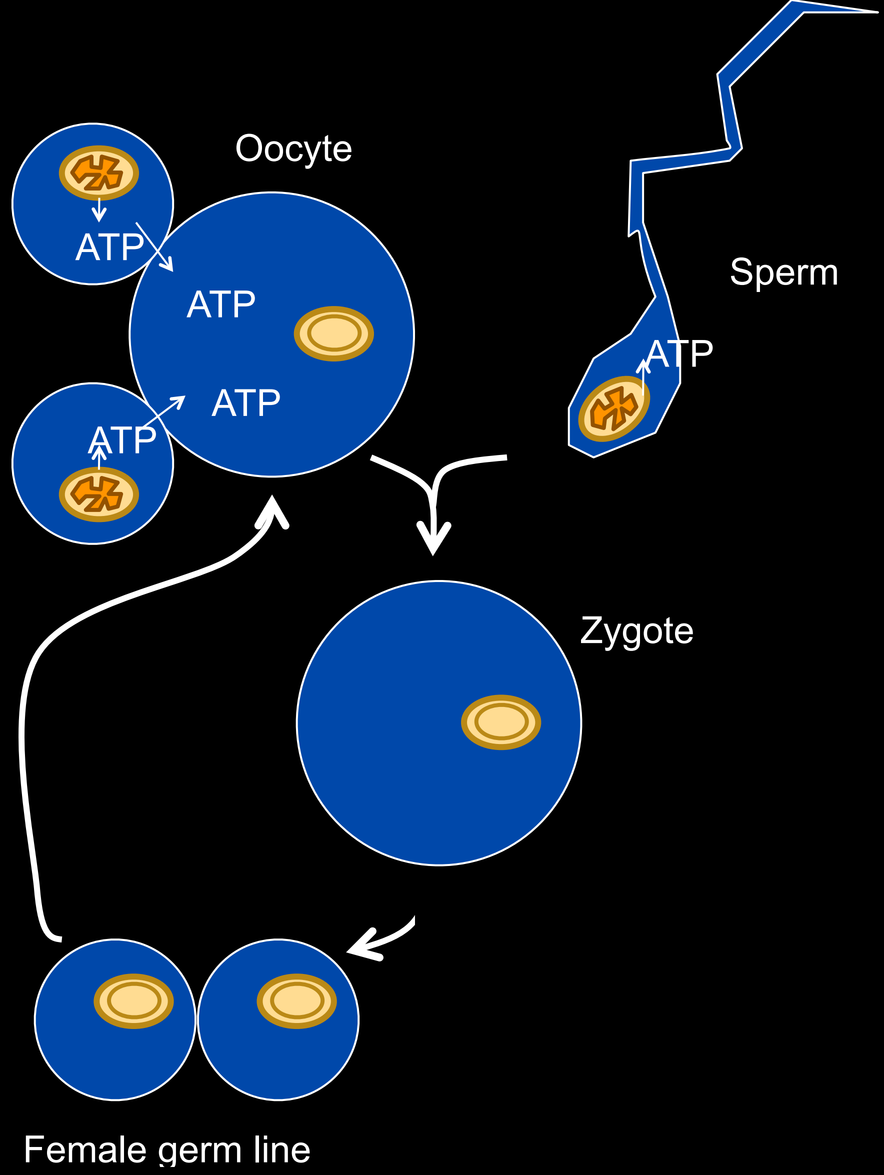
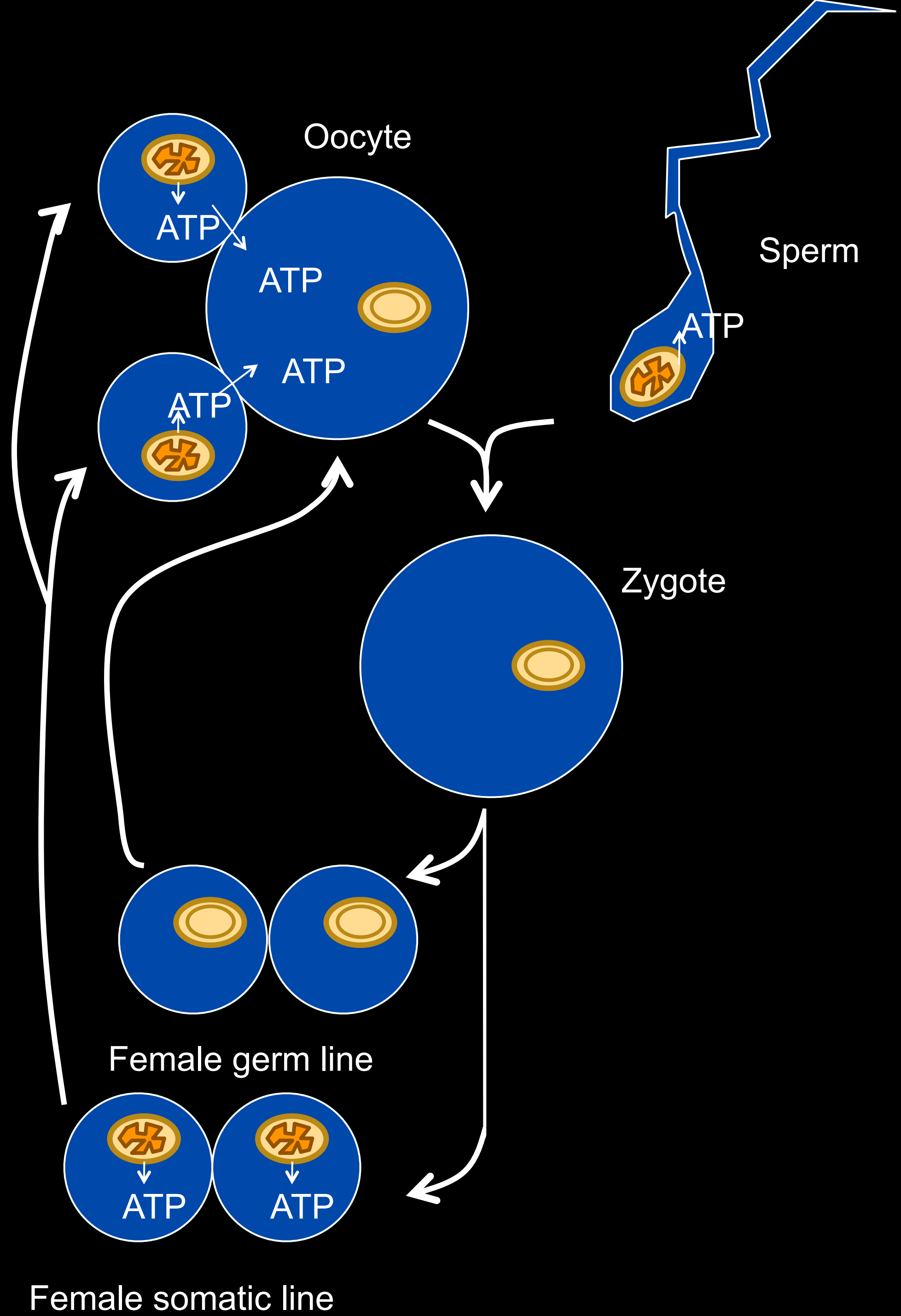
And they can never be both.

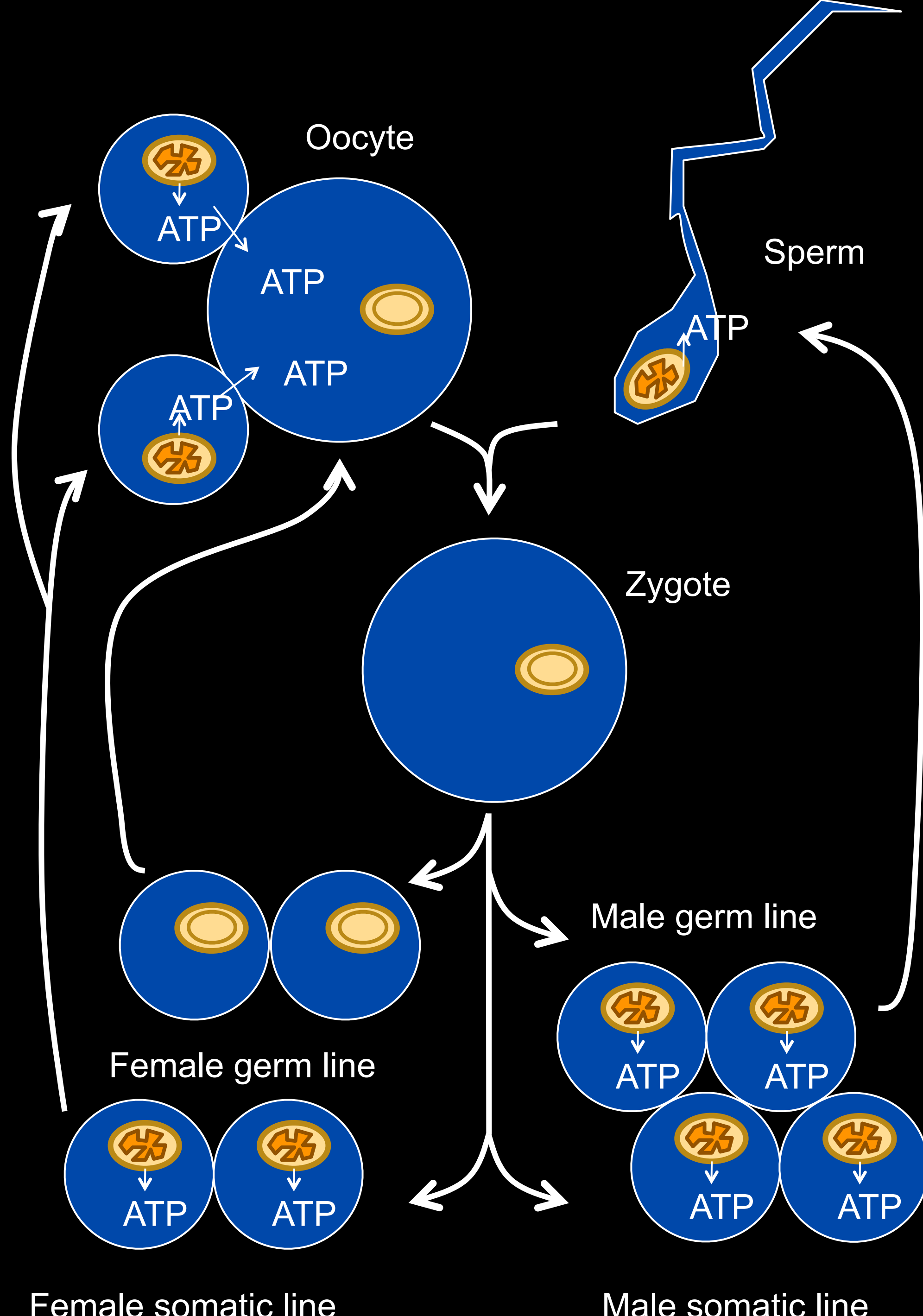

Oocyte
ATP
ATP
ATP
ATP
Sperm
ATP


Oocyte
ATP
ATP
ATP
ATP
Sperm
ATP
Zygote

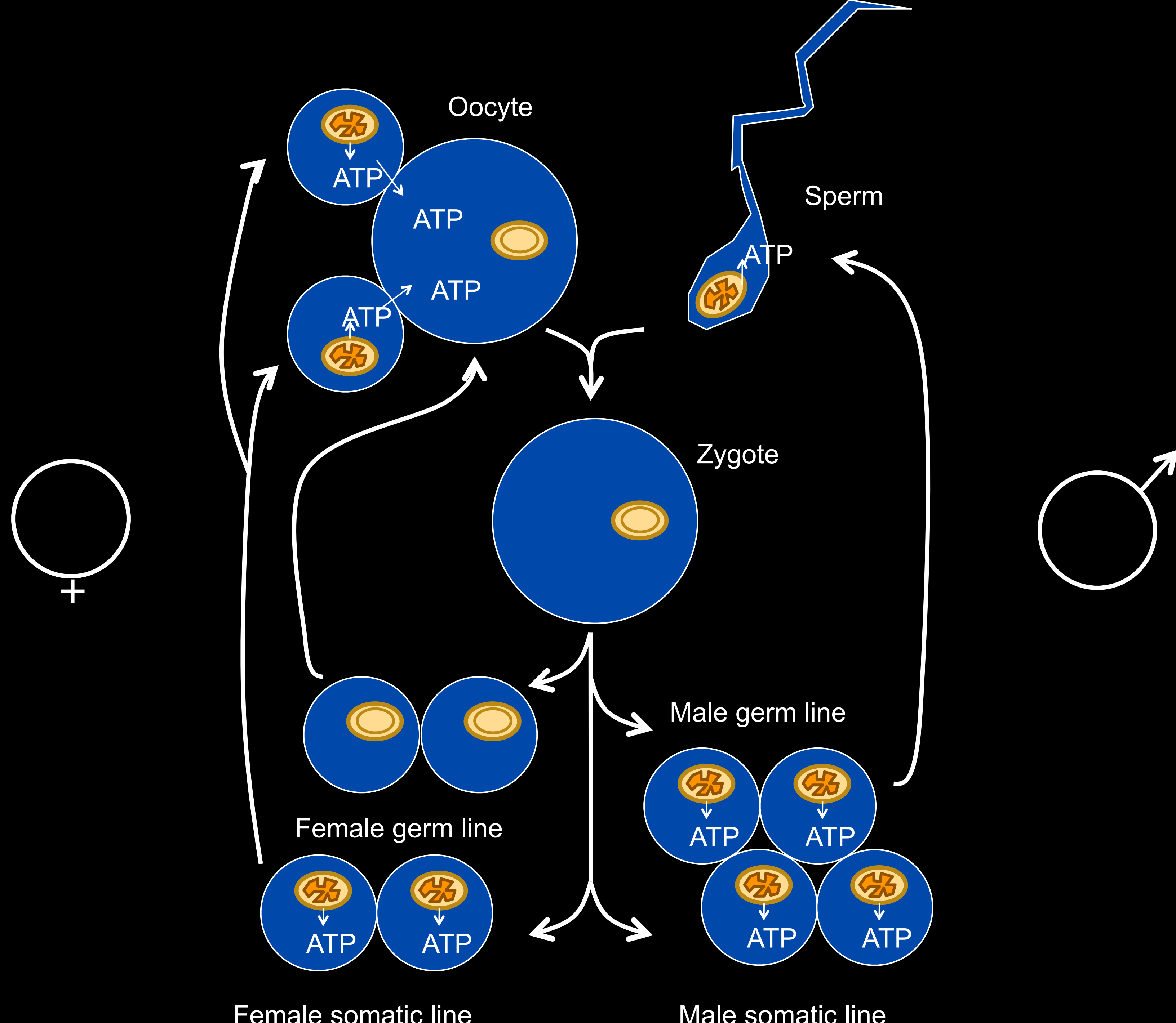

Oocyte
ATP
ATP
ATP
ATP
Sperm
ATP
Zygote
Female germ line



Oocyte
ATP
ATP
ATP
ATP
Sperm
ATP
Zygote
Female germ line
ATP
ATP
Female somatic line



Oocyte
ATP
ATP
ATP
ATP
Sperm
ATP
Zygote
Male germ line
ATP
ATP
ATP
ATP
Female germ line
ATP
ATP
Female somatic line
Male somatic line


Oocyte
ATP
ATP
ATP
ATP
Sperm
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Zygote
Male germ line
ATP
ATP
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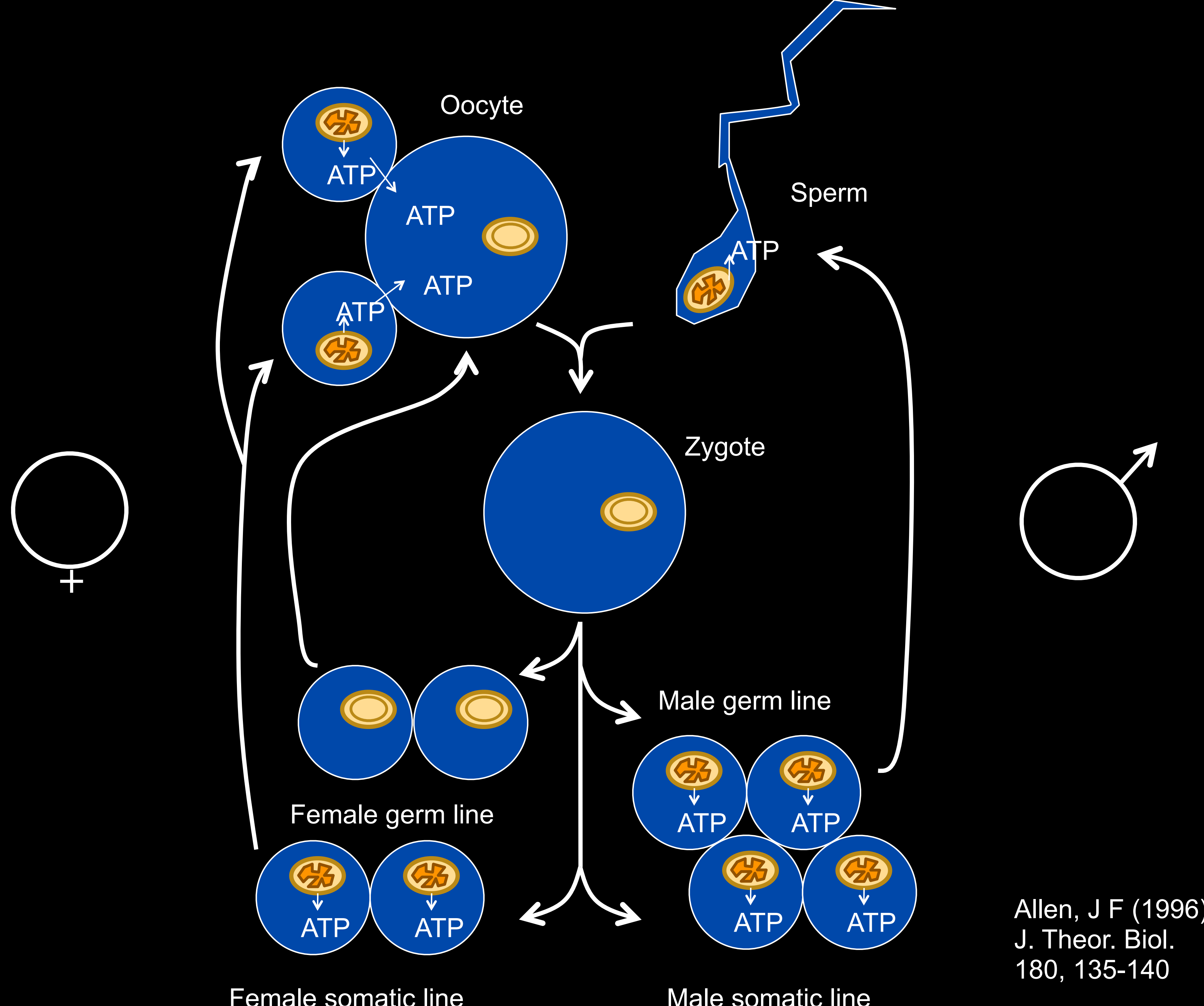
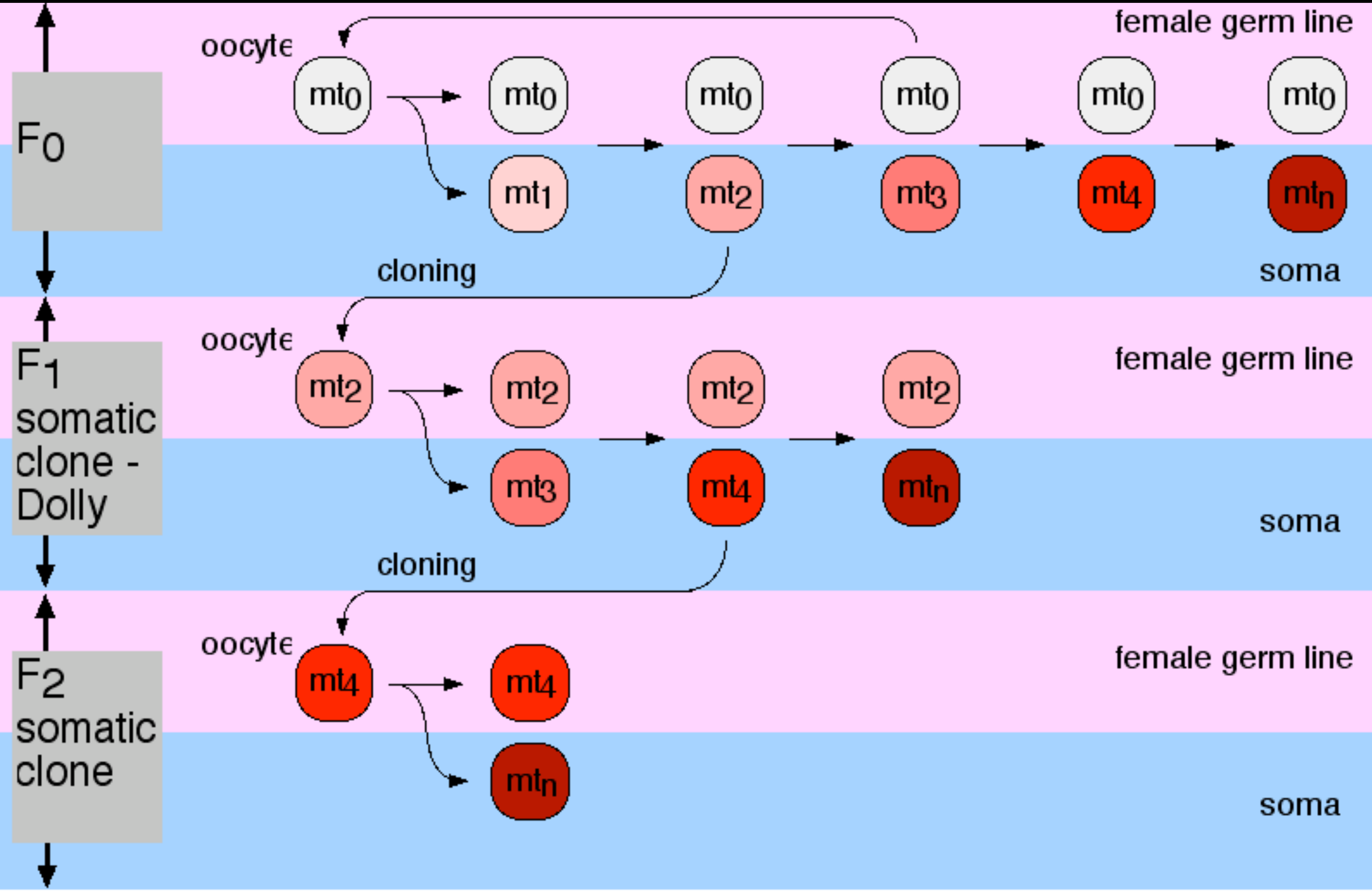
ATP
Female germ line
ATP
ATP
Female somatic line
Male somatic line



Oocyte
ATP
ATP
ATP
ATP
Sperm
ATP
Zygote
Male germ line
ATP
ATP
ATP
ATP
Female germ line
ATP
ATP
Female somatic line
Male somatic line
Allen, J F (1996)
J. Theor. Biol.
180, 135-140



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Dolly, the Finn Dorset ewe, the first mammal to be cloned from an adult cell. Finn Dorset sheep normally live to 11 or 12 years. Dolly had been suffering from lung cancer and died of a drug overdose on 14th February 2003, aged 5. Dolly is survived by three or four of her six lambs.

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Obituary: Dolly the Sheep
http://www.nature.com/nsu/030210/030210-15.html

Separate sexes as mitochondrial division of labour

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– An immortal line of genetic template mitochondria in the female germ line; … from egg back to egg

Summary

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Mitochondria and chloroplasts:

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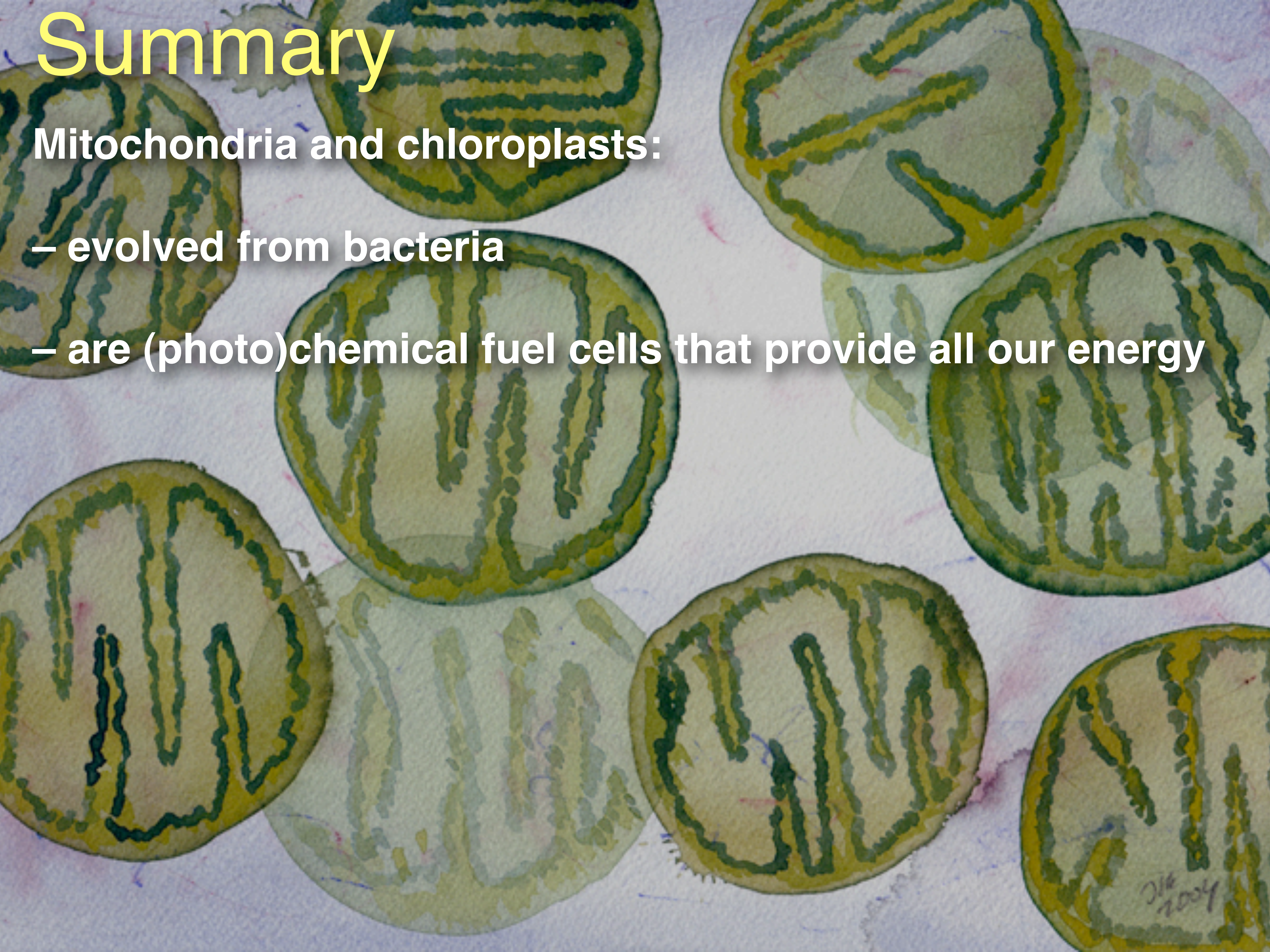

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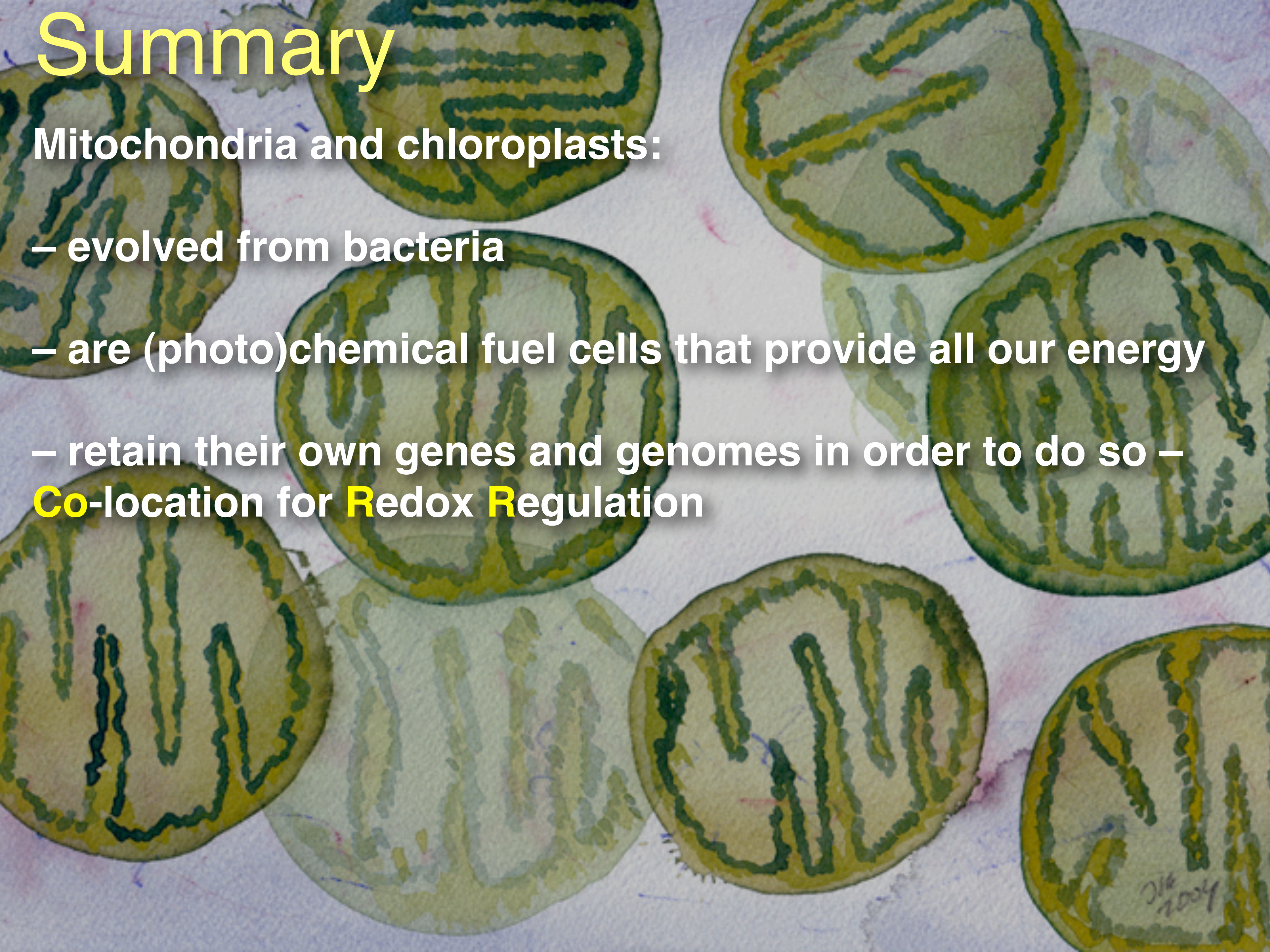

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– are (photo)chemical fuel cells that provide all our energy

– retain their own genes and genomes in order to do so – Co-location for Redox Regulation

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– but might exist also in female germ lines as protected genetic templates, incapable of energy conversion, and from which all other mitochondria and chloroplasts derive

Coda. Two views of mitochondria
View 1

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John Burn (Newcastle Institute of Clinical Genetics). Quoted in *The Times*, 9th September 2005

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– *"…are not part of the genetic material that we consider makes us as human beings."*

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John Burn (Newcastle Institute of Clinical Genetics). Quoted in *The Times*, 9th September 2005

Mitochondria:

– *"…are not part of the genetic material that we consider makes us as human beings."*

"My belief is that what we are doing is changing a battery that doesn't work for one that does.…Changing the mitochondria won't affect the important DNA."

Coda. Two views of mitochondria
View 2

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View 2

Nick Lane. *Power, Sex, Suicide. Mitochondria and the Meaning of Life.* Oxford University Press. 2005.

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View 2

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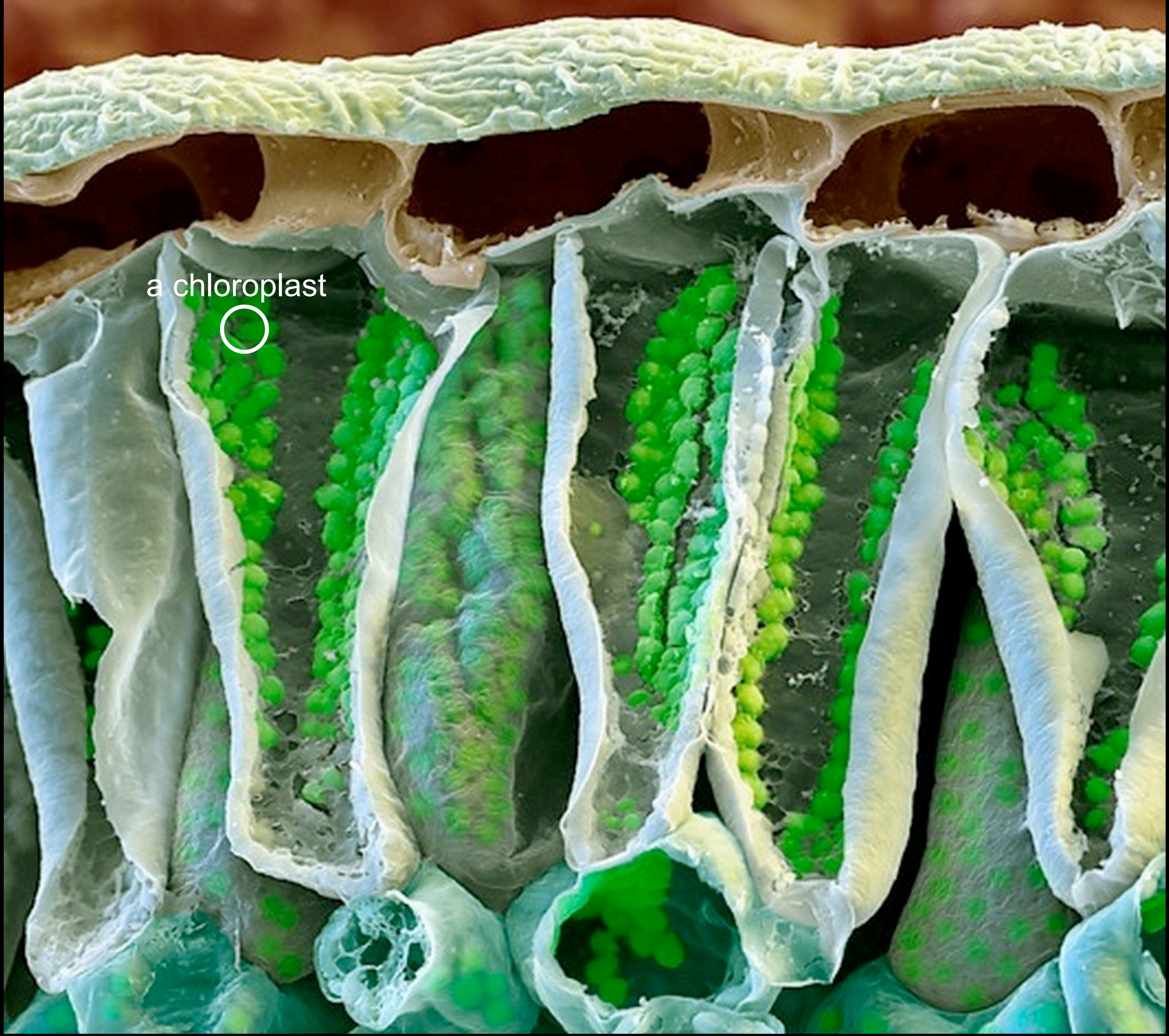
Mitochondria:

– *"…give striking new insights into why we are here at all, whether we are alone in the universe, why we have our sense of individuality, why we should make love, where we trace our ancestral roots, why we must age and die—in short, into the meaning of life."*

A mitochondrion—one of many tiny power-houses within cells that control our lives in surprising ways



‘Christmas-Rose’ leaf SEM cross-section; Science Photo Library (SPL)

Oakwood
Totteridge & Whetstone
Southgate
Theydon Bois
Debden
Loughton
Mill Hill East
Woodside Park
Arnos Grove
Stanmore
Edgware
West Finchley
Finchley Central
Bounds Green
Buckhurst Hill
Roding Valley
Chigwell
Burnt Oak
Canons Park
Colindale
East Finchley
Wood Green
Woodford
Grange Hill
Hainault
Queensbury
Hendon Central
Highgate
Turnpike Lane
Seven Sisters
Blackhorse Road
Fairlop
Kingsbury
Brent Cross
South Woodford
Golders Green
Archway
Manor House
Tottenham Hale
Walthamstow Central
Barkingside
Neasden
Hampstead
Hampstead Heath
Gospel Oak
Tufnell Park
Newbury Park
Dollis Hill
Arsenal
Finsbury Park
Snaresbrook
Redbridge
Willesden Green
Finchley Road & Frognal
Kentish Town West
Kentish Town
Holloway Road
Wanstead
Gants Hill
Kilburn
Belsize Park
Leytonstone
Brondesbury Park
West Hampstead 200m
Chalk Farm
Caledonian Road
Caledonian Road & Barnsbury
Camden Road
Hackney Central
Hackney Wick
Dagenham East
Canonbury
Camden Town
Leyton
Brondesbury
Finchley Road
Swiss Cottage
St. John's Wood
Mornington Crescent
King's Cross St. Pancras
Highbury & Islington
Dalston Kingsland
Homerton
Dagenham Heathway
Upney
Becontree
Paddington
Edgware Road
Baker Street
Great Portland Street
Euston
Angel
Stratford
Barking
Old Street
Farringdon
Barbican
Bethnal Green
Mile End
Pudding Mill Lane
East Ham
Upton Park
Edgware Road
Marylebone
Warren Street
Euston Square
Euston 200m
Regent's Park
Liverpool Street
Plaistow
Bayswater
Goodge Street
Russell Square
Moorgate
Shoreditch
Bow Road
Bow Church 200m
Bromley-by-Bow
West Ham
Holland Park
Queensway
Lancaster Gate
Bond Street
Oxford Circus
Holborn
Tottenham Court Road
Chancery Lane
St. Paul's
Aldgate East
Stepney Green
Whitechapel
Devons Road
Notting Hill Gate
Marble Arch
Bank
Aldgate
All Saints
Bus to London City Airport
Canning Town
Covent Garden
Cannon Street
Shadwell
Westferry
Poplar
East India
High Street Kensington
Hyde Park Corner
Green Park
Leicester Square
Mansion House
Limehouse
Blackwall
Royal Victoria
Piccadilly Circus
Monument
Tower Hill
Fenchurch Street 150m
Tower Gateway
Custom House for ExCeL
Knightsbridge
Charing Cross
Prince Regent
Gloucester Road
Blackfriars
Wapping
West India Quay
West Silvertown
Royal Albert
Sloane Square
St. James's Park
Temple
River Thames
Under construction
Beckton
Rotherhithe
London Bridge
Canary Wharf
West Brompton
Earl's Court
South Kensington
Victoria
Westminster
Embankment
Charing Cross 100m
North Greenwich
Pontoon Dock
Bermondsey
Canada Water
Heron Quays
South Quay
London City Airport
Crossharbour & London Arena
Waterloo
Silvertown
Surrey Quays
Mudchute
Pimlico
Southwark
Waterloo East
Borough
Island Gardens
River Thames
Lambeth North
North Woolwich
Cutty Sark for Maritime Greenwich
New Cross Gate
New Cross
Greenwich
Vauxhall
Elephant & Castle
100m
Deptford Bridge

Queen Mary
University of London

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THE UNIVERSITY OF MELBOURNE

The Botany Foundation


Ebikabowei Bozimo
Carol A. Allen
Iskander Ibrahim
John F. Allen
Azma Shiyam
Thomas Buckland
Sujith Puthiyaveetil


Ebikabowei Bozimo
Carol A. Allen
Iskander Ibrahim
John F. Allen
Azma Shiyam
Thomas Buckland
Sujith Puthiyaveetil
The end. Thank you for listening.